THE NEW PHYSIOLOGY
AND OTHER ADDRESSES.

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PREFACE.

THE addresses collected in this volume refer to different aspects of one subject — the distinctive character of biological knowledge, and its relation to other departments of knowledge. Ideas on this subject, and on the connection of natural science in general with "humanistic" branches of knowledge, are at present, as it seems to me, changing rapidly, and in a direction which is only very imperfectly realised as yet. The scientific theories which dominated the world during the latter half of last century are undergoing profound modification, and the estrangement created by them between natural science and other branches of knowledge is tending to disappear. At the same time new lines of advance in natural science are opening out in all directions, and perhaps most strikingly in biology. For this latter reason I have adopted *The New Physiology* as a title for the book.

In these addresses the claims of biology to an independent position among the sciences are strongly maintained as against the current belief that biology is only applied physics and chemistry. The fourth address

lays special stress on the responsibility of this belief for the present very backward condition of medicine on its therapeutical side. This backwardness has become strikingly evident in connection with the medical problems of the war. The matter is one of great practical importance, and I have endeavoured to indicate the main direction in which reform seems to be needed.

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CONTENTS.

THE NEW PHYSIOLOGY.

I.

THE RELATION OF PHYSIOLOGY TO PHYSICS AND CHEMISTRY.[1]

In deciding to address you on the relation of physiology to physics and chemistry, I am aware that I have selected a subject which has already been treated from this Chair by more than one distinguished predecessor. My excuse for returning to it again is that not only does it possess deep scientific interest for us all, but a great deal remains to be said about it.

The majority of physiologists in recent times have expressed more or less clearly the opinion that physiology is the application to living organisms of the methods and modes of explanation of physics and chemistry. It is, in short, physics and chemistry applied to the activities of living organisms; so that the only explanations aimed at in physiology are, or ought to be, physical and chemical explanations. A minority, who are at present growing in importance, have either definitely dissented from this view, or have remained unconvinced of its truth. As one of this minority, I should like to place before you as shortly as possible what seem to me to be the main reasons of our dissent. Let me add

[1] Presidential Address, Physiological Section of British Association, Dublin, 1908.

that I have carefully pondered over these reasons during many years of active physiological work.

When we look back on the history of physiology, it seems perfectly evident that physiological progress has been dependent on the progress of physics and chemistry. On this point there is no room for doubt. To take only one example, where should we be in the investigation of animal metabolism but for the ideas and experimental methods furnished to us by physics and chemistry? We should know next to nothing about respiration, animal heat, nutrition, or muscular and other work. Physiology depends at every turn on physics and chemistry, and its future progress will certainly be equally dependent on advances in physical and chemical knowledge. This consideration has, I imagine, weighed very heavily in the minds of those physiologists who have concluded that physiology is nothing but applied physics and chemistry. A further fact which weighs equally heavily is that in spite of diligent search nothing contradicting the fundamental laws of conservation of matter and energy has been discovered in connection with living organisms.

When, however, we ask what progress has been made towards the physico-chemical explanation of physiological processes, we at once enter upon controversy. We may point to advances in some directions, but they are accompanied by the appearance of unforeseen difficulties in other directions. Again, to take animal metabolism as a typical instance, the investigations of the last hundred and twenty years have enabled us to assign ultimate physical and chemical sources to the energy and material leaving the body in various forms. We

can assign to such sources the energy of animal heat, muscular work, glandular, nervous, and other activity: also the carbon dioxide, urea, salts, and many other substances which leave the body or are formed within it. All of this new knowledge may be regarded as progress towards a physico-chemical explanation of life.

But there is another aspect to be considered; for side by side with what I have just referred to there has been a different kind of increase of knowledge with regard to animal metabolism. This growth of knowledge relates to the manner in which the passage of energy and material through the body is regulated in accordance with what is required for the maintenance of the normal structure and activities of the body. In Liebig's time, for instance, it was believed that the rate of respiratory exchange was regulated simply by the supply to the body of oxygen and food material. If one breathed faster, or if the barometric pressure or percentage of oxygen in the air increased, the respiratory exchange was assumed to be also increased, just as ordinary combustion outside the body would be increased by an increased supply of oxygen. If, again, one took in more food, it was supposed that the excess went to increase the rate of combustion in the blood (*luxus consumption*), just as a fire is increased when more fuel is supplied. We now know that these assumptions were wholly mistaken, and that the respiratory movements, respiratory exchange, and corresponding consumption of food material in the body are regulated with astounding exactitude in accordance with bodily requirements. If, for instance, the body consumes more protein, it economises a quantity of fat or carbohydrate equivalent in energy value to the

protein, and from day to day the amount of energy liberated in the body is very steady. With regard to the excretion of material by the kidneys a similar growth in knowledge can be traced. It is scarcely a century since the urine was regarded as equivalent more or less to the liquid part of the blood separated from the corpuscles, which were unable to pass through the very fine capillary tubules supposed to exist in the kidney substance. Gradually, however, we have learnt how extraordinarily delicate is the selective action which occurs in the kidney substance, and how efficiently this selective action maintains the normal composition of the blood. Scarcely a remnant is now left of the old filtration theories. Our ideas of tissue nutrition and growth have undergone a similar change ; and it is hard to realise that only about seventy years ago Schwann could put forward the theory that cell formation and growth is a process of crystallisation.

One can multiply instances like these almost indefinitely ; but I have, perhaps, said enough to show that if in some ways the advance of physiology seems to have taken us nearer to a physico-chemical explanation of life, in other ways it seems to have taken us further away. On the one hand, we have accumulating knowledge as to the physical and chemical sources and the ultimate destiny of the material and energy passing through the body : on the other hand, an equally rapidly accumulating knowledge of an apparent teleological ordering of this material and energy ; and for this teleological ordering we are at a loss for physico-chemical explanations. There was a time, about fifty years ago, when the rising generation of physiologists in their

enthusiasm for the first kind of knowledge closed their eyes to the second. That time is past, and we must once more face the old problem of life.

Let us first look at the answer given to this problem by many of the older physiologists. Roughly speaking, they carried physical and chemical explanation of physiological processes as far as they could, and for the rest assumed that at some point or other the physical and chemical factors are interfered with and ordered in a teleological direction by something peculiar to living organisms—the "vital principle" or "vital force." This theory, if one can call it a theory, had the negative merit that it did not lead physiologists to ignore facts which they could not explain. In practice the "vital force" became simply a convenient resting-place for these facts. It was assumed that the vital force can do anything and everything, and that it acts "from the blue" on physical and chemical processes. But its action was admittedly dependent on physical and chemical conditions, such as warmth, the presence of oxygen, etc. In fact no consistent definition was given to the conception of "vital force." It consequently never could become a working hypothesis of any value. Chiefly on this account, I think, it practically disappeared from physiology last century. Yet the class of fact which led to the theory of "vital force" is now more prominent then ever; and what du Bois-Reymond called the "spectre" of vitalism meets us at every turn, thinly disguised under such names as "cell autonomy," "vital processes," etc. It is useless to shut our eyes and deny the existence of this "spectre." We must fairly face and examine it.

However difficult it may be to imagine physico-chemical explanations of such processes as respiratory exchange, secretion, muscular activity, etc., there is nothing in the known facts relating to each process taken by itself to preclude the possibility of such explanations. Let us then follow the Euclidean method and assume, provisionally, that they are nothing but physico-chemical processes. This assumption evidently implies that each of the living cells concerned has a very complex and definite structure varying according to its functions. To take an example, a secreting cell in the kidney may be assumed to have a structure which responds to the stimulus of a certain percentage of urea or sodium chloride in the blood, and reacts in such a manner that energy derived from oxidation is so directed as to perform the work of taking up urea or sodium chloride from the blood and transferring it against varying osmotic pressures from one side of the cell to the other. This mechanism must also be assumed to have the property of maintaining itself in working order, and probably also of reproducing itself under appropriate stimuli, besides also performing various other functions. Its physico-chemical structure must thus be very definite and complex—to an extent which the older physico-chemical theories took no account of. If we look to the cells in other parts of the body, we are met with the same necessity for assuming complexities of structure which seem to grow in extent with every advance in physiological knowledge, every discovery of new substances present within or around the cells, every discovery of new physiological reactions.

Let us not lose courage, however, but continue to

follow the direction in which our assumption leads. In assuming that the body is an enormously complex physico-chemical structure, we have only begun to face the difficulties of our hypothesis: for we have still to consider how this structure can have originated in accordance with the physico-chemical theory of life. The adult organism develops from a single cell, the fertilised ovum. It is certain that this cell does not contain in a preformed condition the structure of an adult organism. The conditions of environment in which any particular ovum develops itself are doubtless indefinitely complex from the physico-chemical standpoint, as indeed is the environment of any particular portion of matter existing anywhere. But these conditions also vary almost indefinitely in the case of different ova, whereas the adult organism to which the ovum gives rise reproduces in minute detail the enormously complex characters of the parent organism. We are thus driven to the assumption that the ovum contains within itself a structure which, given certain relatively simple conditions in the environment, reacts in such a way as to build up step by step, from materials in the environment, the structure of the adult organism. To effect this the germ-cell must have a structure almost infinitely more definite and complex than that of any cell in the adult organism. Difficult as it may be to form any conception of the mechanism of a secreting cell, it is infinitely more difficult to form the remotest idea of that of a germ-cell.

But we are still only at the beginning of the difficulty. The assumed tremendous mechanism of the germ-cell has been developed, together with the whole of the rest of the parent organism and countless other germ-cells,

from a previous germ-cell. What must the "mechanism" of this cell have been? And that of its endless predecessors? We have reached the Euclidean *reductio ad absurdum*.

I might strengthen my argument by referring to the further difficulty over any physico-chemical conception of what occurs in the sexual fusion of the male and female cell, or in the process of partial reproduction after injury, or in the facts established by Driesch and others with regard to the extraordinary reproductive powers of each cell in developing embryos. But I have purposely confined my references to more simple and well-known facts; for the more simply the argument can be put, the better. I confess that as a physiologist I am struck with amazement at the manner in which heredity is often discussed by contemporary writers who endeavour to treat the subject from a mechanistic standpoint. Sometimes, indeed, the germ-cell is acknowledged to be a complicated structure, but at other times it is treated as a "plasma," which can be mixed with other "plasma," divided, or added to, as if for all the world it were so much treacle! I have tried to place clearly before you the assumptions in connection with heredity which, to my mind, make the physico-chemical theory of life unthinkable, even if it be tenaciously clung to in connection with those ordinary physiological phenomena where, as already explained, it has proved so disappointing.

Our aim as physiologists is to render physiological phenomena intelligible—in other words, to obtain general conceptions as to their nature. The point now reached is that the conceptions of physics and chemistry are in-

sufficient to enable us to understand physiological phenomena. But if so, we need not sit down in despair, for we can look for other working conceptions. Are we justified in doing this ? I think we are.

There is a prevalent popular idea that the world as presented to us under the conceptions of physics and chemistry is more than our own imperfect conception of reality, and corresponds completely with reality itself. Philosophy has shown us, however, that this idea must be erroneous ; for if it were correct, knowledge of such a world would be impossible. This was first clearly pointed out almost two hundred years ago in this city by one of the greatest of Irishmen, George Berkeley, at that time a Fellow of Trinity College.[1] The lesson taught by Berkeley, Hume, and their successors is not that physical science is of less value than it appears to be, but that its fundamental hypotheses are only working hypotheses, applicable only so far as they successfully fulfil their purpose. Each different science is thus free to employ whatever working hypotheses may prove most useful in interpreting the order of phenomena with which it deals. We are thus perfectly justified in seeking to find a conception of life which will serve as a better working hypothesis than that of life as a physico-chemical process.

I venture to think that the conception we are in search of lies very near to hand, and is indeed in common use, though in a form which has hitherto been too ill-defined for deliberate scientific employment. It is simply the conception of the living organism, which stands, or ought to stand, in the same relation to biology as the

[1] *Treatise concerning the Principles of Human Knowledge*, 1710.

conceptions of matter and energy to physics, or of the atom to chemistry. Let me try to give more definition to this conception. A living organism is distinguished by the fact that in it what we recognise as specific structure is inseparably associated with what we recognise as specific activity. Its activity expresses itself in the development and maintenance of its structure, which is nothing but the expression of this activity. Its identity as an organism is not physical identity, since from the physical standpoint the material and energy passing through it may be rapidly changing. In recognising it as an organism, we are applying an elementary conception which goes deeper than the conceptions of matter and energy, since the apparent matter and energy contained in, or passing through, or reacting with, the organism are treated as only the sensuous expression of its existence. Even the environment is regarded as in organic relation with the organism, and not as a mere physico-chemical environment. It follows that for biology we must clearly and boldly claim a higher place than the purely physical sciences can claim in the hierarchy of the sciences—higher, because biology is dealing with a deeper aspect of reality. It must also be the aim of biology gradually to penetrate behind the sensuous veil of matter and energy which at present seems to obscure the organic world at all points.

Let us now see how the conception just defined can be used as a scientific working hypothesis. In accordance with it any form of physiological activity is presumably related essentially, and not accidentally, to the other details of activity and structure in the same organism. Stated generally, therefore, the problem of

physiology is not to obtain piecemeal physico-chemical explanations of physiological processes, but to discover by observation and experiment the relatedness to one another of all the details of structure and activity in each organism as expressions of its nature as an organism.

The first step in physiological or morphological discovery is to observe the bare sensuous fact of some detail of physical or chemical change, or of composition or structure, in connection with an organism. It is only, however, when we find that this detail is not accidental that it becomes of biological interest. We can observe its constancy or otherwise in the same organism or similar organisms—that is to say, the constancy of its relations to other details of structure and activity. We can also by experiment search for the element of constancy when it is at first sight hidden from our view. In so far as we find this, it seems to me that we reach physiological or biological explanation; but evidently the process of reaching it is at any stage in knowledge only imperfectly realised, since new details of activity and structure are constantly being revealed.

Concrete examples will make the matter clearer, and I shall first take as an example the progress of knowledge in relation to animal heat. It was of course common knowledge from early times that in the higher animals a certain amount of warmth in the body is present during life. With the invention of the thermometer the body-temperature could be measured, and its extraordinary constancy observed. When Lavoisier measured the heat-production of an animal, and compared the output of heat with the output of

carbon dioxide and disappearance of oxygen in respiration, an immense step forward was taken. This step was in two distinct respects a very great one. In the first place, it revealed an element of identity between organic and inorganic phenomena, since heat-production in an animal was shown to be accompanied by chemical changes quantitatively identical with those accompanying heat-production by oxidation outside the body. In the second place, and from the distinctively physiological point of view, it revealed a fundamental relation between heat-production, respiratory exchange, and the consumption of food.

As regards the first of these points I should like to say definitely that I, for one, firmly believe that could we only understand them fully we could bring organic and inorganic phenomena under the same general conceptions. Lavoisier's discovery, like that of Mayer in relation to the sources of muscular energy, was a great advance in this direction. But this is a very different thing from an advance in the direction of rendering life intelligible in terms of physico-chemical conceptions as we commonly understand them. Lavoisier's discoveries did nothing in the direction of reducing to physico-chemical terms the apparent teleological or, as I should prefer to say, "physiological" element in the phenomena of animal heat.

It is to the second point that I wish to direct special attention at present. Lavoisier's discovery rapidly brought the phenomena of animal heat into direct relation, not only with respiration but with nutrition, circulation of blood, excretion, and other processes; and it was gradually discovered that the maintenance

of a constant body-temperature renders physiologically intelligible a large number of phenomena in connection with different bodily activities—for instance, increased metabolism with fall of external temperature, sweating or increased circulation through the skin with muscular work, the relative constancy of metabolism during starvation, and the physiological equivalence of protein, carbohydrate, and fat in proportion to their energy values. These phenomena are intelligible on the assumption that warm-blooded animals actively maintain a certain body-temperature, just as they maintain a certain bodily structure and composition. This mode of explanation is not a physico-chemical one, but I venture very confidently to assert that it is a physiological one, and in fact the only kind of explanation which really interests and appeals to a true physiologist. The thread of identity which has been traced through the phenomena just referred to seems to me to have proved a real scientific clue.

As another example I may perhaps be allowed to refer shortly to the regulation of breathing, as this is a subject on which I have recently been working. Current accounts of the clock-like action of the respiratory centre during normal breathing, with the expansion and contraction of the lungs acting as a sort of governor through the vagus nerves, always filled me with suspicion, as it seemed to me that such a regulation was altogether unlike a physiological one. This led me to investigate the matter further, along with Mr Priestley; and we had the satisfaction of being able to prove that the ventilation of the lungs is actually regulated with exquisite exactness, in such a way as to keep the partial

pressure of carbon dioxide in the alveolar air, and presumably, therefore, in the arterial blood, constant. In reality, therefore, the lung ventilation is regulated in accordance with the requirements of respiratory exchange; and what seems to be true physiological explanation has been advanced a short stage.

The advance of knowledge with regard to the circulation might be made the text of a similar discourse. By a process of abstraction the circulation of the blood may be regarded as a mere mechanical process, connected only by the accidents of physical structure with other physiological processes. Under the influence of mechanistic theories the blood-pressure and rate of blood-flow through different organs were indeed for long supposed to be the primary determining cause of the physiological activities of these organs, just as the rate and depth of breathing were supposed to determine the consumption of oxygen by the body. Evidence is, however, accumulating on all hands, that the blood-supply to various parts, like the air-supply to the lungs, is in reality determined by physiological requirements. In other words, it is a direct expression of the nature of the organism, just as the common-sense idea of life would lead us to expect.

I may pass next to a branch of physiological knowledge which is still in its early infancy. Under the influence of mechanistic ideas physiology has for long left completely out of account investigation into the formation and maintenance of organic structure. For mechanistic explanations structure had to be assumed, and as a consequence anatomy was left high and dry in a position of helpless isolation. If, however, the real

aims of physiology are those which I have tried to indicate, the separation between physiology and anatomy must tend to disappear: for the structure no less than the activity of each part must be determined by its relations to the structure and activities of other parts in the organic whole of the living organism. We can investigate these relations, just as we investigate the connection of secretion with respiratory exchange, circulation, or the composition of the blood; and they must evidently be physiological relations. Our aim is not the hopeless one of giving a physico-chemical explanation of the development and maintenance of organic structure, but simply to discover the physiological relations which determine the structure of each part and its maintenance. Many facts bearing on this subject have recently been brought to light by the application of experimental methods to embryology, and by the study of reproduction of lost or injured parts, and of grafting: also by the study of so-called "internal secretion" in connection with various organs. It seems clear, however, that we are only at the beginning of a vast development of knowledge in this direction, and that for this development far more refined methods of dealing with the chemistry of the body will be required.

It was in connection with the facts of reproduction and heredity that the difficulties of the mechanistic theory of life were found finally to culminate. For the distinctively biological theory of life, to which I have endeavoured to give some definition, these difficulties do not exist. They are, it is true, not solved; but they are set aside as being due to wrong initial assump-

tions and therefore purely artificial. The difficulty remains of reconciling the fundamental conceptions of biology with those of physics and chemistry. This is, however, a matter of which the discussion must be handed over to philosophy, which has many similar matters to deal with. If it is a fundamental axiom that an organism actively asserts or maintains a specific structure and specific activities, it is clear that nutrition itself is only a constant process of reproduction: for the material of the organism is constantly changing. Not only is there constant molecular change, but the living cells are constantly being cast off and reproduced. It is only a step from this to the reproduction of lost parts which occurs so readily among lower organisms; and a not much greater step to the development of a complete organism from a single one of the constituent cells of an embryo in its early stages. In all these facts we have simply manifestations of the fundamental characters of the living organism. The reproduction of the parent organism from a single one of its constituent cells separated from the body seems to me only another such manifestation. Heredity, or, as it is sometimes metaphorically expressed, organic memory, is for biology an axiom and not a problem. The problem is why death occurs, what it really is, and why only certain parts of the body are capable of reproducing the whole. These questions carry us, at least in part, beyond the present boundary lines of biology. They involve those ultimate questions which, as has just been pointed out, it is the province of philosophy to deal with.

To turn to another set of questions, the distinctively

biological standpoint in biology involves a change in what has in recent times become the ordinary attitude towards organic evolution. Since our conception of an organism is different in kind, and not merely in degree, from our conception of a material aggregate, it is clear that in tracing back life to primitive forms we are getting no nearer to what is called abiogenesis. The result of investigation in this direction can only be to extend further the domain of biology and widen biological ideas. Our aim must be, in short, not to reduce organic to inorganic phenomena, but to bring inorganic phenomena into the domain of biology.

I am well aware that it will be strongly maintained that the change of front which I have urged as necessary involves the giving up of all real attempt at scientific explanation in biology. As already explained, this is a philosophical question, and I shall not attempt to deal further with it here. What immediately concerns us as biologists is whether the change of front will further or hinder biological advance, particularly in physiology. Now the first requisite of a working hypothesis is that it should work, and I have tried to point out that as a matter of fact the physico-chemical theory of life has not worked in the past and can never work. As soon as we pass beyond the most superficial details of physiological activity it becomes unsatisfactory; and it breaks down completely when applied to fundamental physiological problems such as that of reproduction. Those who aim at physico-chemical explanations of life are simply running their heads at a stone wall, and can only expect sore heads as a consequence. It seems to me that the proposed change of front is only the con-

scious adoption of a common-sense idea which is somewhat vaguely, perhaps, present in the minds of all men, and which has in reality guided biological advance in the past. This idea, as I have tried to show, is a working hypothesis which actually works, and affords clear guidance for future advance.

I would fain add a few words as to the relation of physiology to psychology and ethics: for this is a subject of deep human interest. We know that at any rate the higher organisms are conscious and intelligent. This fact brings physiology into touch with a new element in the behaviour of organisms. The subject is far too great a one for me to attempt to discuss here, but I should like to say that it appears to me very clear that just as biology is something more than physics and chemistry, so psychology is something more than physiology with the added assumption that consciousness is tacked on to certain physiological processes, if such a crude conception has any definite meaning. We can, it is true, by a process of abstraction treat sensation from the purely physiological side, as in investigating the physiology of the sense-organs; but this is physiology and nothing else; for we are leaving out of account the distinctive elements of consciousness. At our present stage of knowledge life is not intelligence, and men or animals as intelligent individuals involve a deeper aspect of reality than biology deals with. Our fundamental physiological working hypothesis cannot be successfully applied to the phenomena of intelligence, and the sooner and more definitely this is realised the better for physiology.

In conclusion, let me endeavour to state shortly the

main contention which I have endeavoured to place before you. It is that in physiology, and biology generally, we are dealing with phenomena which, so far as our present knowledge goes, not only differ in complexity, but differ in kind from physical and chemical phenomena; and that the fundamental working hypothesis of physiology must differ correspondingly from those of physics and chemistry.

That a meeting-point between biology and physical science may at some time be found, there is no reason for doubting. But we may confidently predict that if that meeting-point is found, and one of the two sciences is swallowed up, that one will not be biology.

II.

THE PLACE OF BIOLOGY IN HUMAN KNOWLEDGE AND ENDEAVOUR.[1]

WE meet in the shadow cast by the greatest war in human history. To many of us that shadow is specially deep. We see our fellow-men willingly offering their own lives, and the lives of their best and dearest, for great ideals. The main problems as to the meaning of human life and endeavour are thus thrust upon us, and specially on those who have to remain behind.

We are a body of scientists or of persons interested in, and willing to devote such time as we can to science. What, in the last resort, are our aims, and are they worthy aims? This is the question which I wish to bring before you to the best of my ability, and with special reference to biology, and more particularly the physiological side of it—the branch of science on which I feel most qualified to speak.

Many persons would, I think, incline to the opinion that science is essentially the pursuit of pure truth, apart from any practical needs and interests; and that while the practical applications of scientific discovery are all to the good, the real aims of science are altogether

[1] Presidential Address, South-Eastern Union of Scientific Societies, June 1915.

unconnected with practical applications. There is evidently much to be said in support of this view. The Societies represented at this meeting are certainly not devoted to what would ordinarily pass for practical objects, and the interest which attracts so many persons to science does not on the surface appear to be a practical interest.

It is nevertheless equally true that scientific work excites our emotions in a high degree—a fact difficult to explain if we are only pursuing the bare truth about facts which in no way enter into our lives. What does it matter to us, for instance, whether certain stimuli cause an Arcella to produce bubbles of gas within its protoplasm, or what gas these bubbles consist of? Yet why does such a problem seem to physiologists so interesting as a matter of fact? And why are we not equally interested in endless other occurrences which are constantly taking place around us, and about which, if we were only seeking for abstract truth, we might be expected to be equally interested? Something is evidently lacking in our provisional definition of the aims of science, and we must try to get nearer to this something.

Let me try to follow out the case of the gas-bubbles in the Arcella. Perhaps I may remind you that *Arcella vulgaris* is a microscopic unicellular organism found in rivers and ponds. It has a more or less transparent shell, shaped something like the top of a mushroom, with an opening where the stalk would come. Through this opening it protrudes delicate pseudopodia, by means of which it can creep about. When a living and healthy Arcella is examined in a drop of water under the micro-

scope, the presence of one or more gas-bubbles inside its protoplasm can at times be observed, particularly if by accident or design the animal has been turned on its back, with the opening of its shell upwards. The bubbles of course make the animal lighter, so that it rises towards the surface of the water, and also comes right side up, after which they rapidly disappear again. The occurrence of these phenomena was described many years ago by Engelmann. Quite recently Dr Bles took up the subject again at my suggestion, and elicited the very interesting fact that a comparatively slight deficiency in the normal oxygen percentage of the water causes the animal to develop bubbles at once, and come to the surface.

Now this is apparently a case of visible and easily observed intra-protoplasmic gas-secretion, and for various reasons it is probable that the gas liberated is oxygen. The occurrence of oxygen-secretion was already known, as an isolated fact, in the case of the swim-bladder of the fishes. The original discovery of this was made over one hundred years ago by the French physicist and chemist Biot. Being engaged in some survey work on the Mediterranean, he was attracted by the observation that deep-sea fishes caught with a line at great depths come to the surface with their swim-bladders distended with gas, or even bursting. Led by a sure scientific instinct, he determined to analyse the gas, but expected it to be something like air in composition. He added hydrogen to some of the gas in a eudiometer and passed a spark, in order to determine the oxygen in the usual way. But instead of the ordinary mild explosion in analyses of air there was a violent explosion

which broke his instrument. He then knew that he had made a most significant discovery, as the gas he was dealing with must be nearly pure oxygen; so he got another eudiometer and with proper precautions made a large number of analyses, which he published in the *Mémoires de la Société d'Arcueil* of 1807. These analyses showed that the greater the depth from which a fish was taken the more nearly did the gas from the swim-bladder approximate to pure oxygen.

A long time elapsed before the significance of Biot's discovery was realised by physiologists, and it was seventy years later before the subject was again effectively taken up in a very interesting monograph by Moreau,[1] a French physiologist. He showed experimentally what the real functions of the swim-bladder are; while later physiologists have added many further contributions on which I must not stop to dwell. Perhaps the most noteworthy of these is the discovery by Bohr of Copenhagen that the secretion of oxygen is under the control of the nervous system, the secretory nerve being a branch of the vagus.

As nearly pure oxygen has been obtained from the swim-bladders of fishes living at a depth of 4500 feet, it follows that oxygen may be secreted into the swim-bladder and retained in it in the gaseous form at a pressure of over 120 atmospheres, whereas the partial pressure of oxygen in the surrounding sea-water is only about one-fifth of an atmosphere. It seems perfectly clear, therefore, that the liberation of oxygen and its retention by the semi-liquid wall of the swim-bladder is the result of an active physiological process in the

[1] *Mémoires de physiologie*, Paris, 1877.

living cells lining its walls, and cannot be explained mechanically.

The case of the swim-bladder threw grave doubt on the current mechanical explanation of the absorption of oxygen into the blood through the epithelial cells lining the alveoli of the lungs; for this might also be partly or wholly a case of active absorption and not of mere diffusion. The question was taken up by Bohr and others, but the evidence was not conclusive. Experiments with improved methods by Krogh[1] of Copenhagen, and by Douglas and myself[2] at Oxford, then showed that under normal resting conditions the phenomena are consistent with the diffusion theory. Our own experiments gave, however, the clear result that under conditions where oxygen-want is produced in the tissues, active absorption occurs. Perhaps the most striking results were obtained as the outcome of an expedition to the summit of Pike's Peak, Colorado, in order to observe to what extent, and by what means, acclimatisation to diminished atmospheric pressure occurs.[3] It was experimentally shown many years ago by Paul Bert in his book *La pression barométrique*, Paris, 1878, that the various physiological disturbances, such as mountain sickness, associated with exposure to diminished atmospheric pressure, are due to want of oxygen, depending on the fact that although the oxygen percentage in air at high altitudes is precisely the same as elsewhere, the partial pressure of the oxygen in the

[1] *Skand. Archiv für Physiologie*, xxiii. p. 179, 1910.

[2] *Journal of Physiology*, xliv. p. 305, 1912.

[3] Douglas, Haldane, Henderson and Schneider, *Philosophical Transactions*, B, vol. 203, p. 185, 1913.

air is diminished in proportion to the fall of atmospheric pressure. Paul Bert's conclusions have again and again been attacked or misunderstood by subsequent writers, but as to their substantial correctness there is not now a shadow of doubt.

We selected Pike's Peak for the observations because of the existence of a cog-wheel railway to the summit at 14,100 feet, and a substantial building, in which we were promised, and were given, excellent accommodation for ourselves and all our apparatus, and where we had ample opportunities of observing the effects of the air on the numerous people who came up. When we first went up we were, like other newcomers, slightly blue in the lips and face, and after a few hours began to suffer from the very unpleasant symptoms of mountain sickness. In the course of the next two or three days these symptoms of oxygen-want passed off, and though we were still unusually short of breath after muscular exertion, we remained extremely well, and of a perfectly normal colour, like the other persons living on the summit. There was thus no doubt about the acclimatisation. Our measurements now showed that the partial pressure of oxygen in the arterial blood was considerably higher than in the air of the lung alveoli. An active secretion of oxygen inwards into the blood had thus established itself, even during rest; and on this active secretion the main phenomena of acclimatisation depend, so far as we could judge. But for this active secretion it would be hard to understand, for instance, how the Duc d'Abruzzi and his party could have climbed in deep snow to a height of 24,600 feet in the Himalayas. Even on Pike's Peak at only 14,000

feet many people who came up fainted from want of oxygen, and we could revive them promptly by administering pure oxygen.

It has thus been established that living animal cells, and not merely living and chlorophyll-containing vegetable cells, have the power of liberating or secreting free oxygen. This is an important scientific generalisation, which will certainly be used as a lamp for guiding future investigation, and may also be of practical importance, for instance in medicine. The same may be said of all scientific generalisations; but it would be absurd to claim that all, or indeed any considerable proportion, of scientific work has immediate practical objects. We certainly did not go to Pike's Peak as medical philanthropists. I can remember a secret spasm of joy when a newcomer with blue lips and tottering legs challenged one of us to a pugilistic encounter, and I thus recognised the psychological symptoms of want of oxygen, familiar to me already through experience of carbon monoxide poisoning in mines. I fear also that we behaved with arrant hypocrisy to a newspaper representative who came to ask for an interview. We were about to express our great regret that we were too busy, when we noticed that he was particularly blue and rather shaky. We immediately asked him to come in, and proceeded to ply him with "copy," waiting until both his hands and legs gave way. Meanwhile we had some oxygen ready, and with much show of sympathy got him to breathe it when he was just on the point of fainting. To our great satisfaction his lips became red again, and he entirely revived, after which we again continued the interview, and again had the satisfaction of seeing

him blue and faint, and revive with oxygen, though after this he felt he had had enough of Pike's Peak, and made a sudden bolt for a car which was just starting downwards.

The case of oxygen secretion has a far wider interest than those of practical medicine, and I must now try to follow this wider interest. At present there are two very different views as to the aims and tendencies of biological investigation. The first view, which the present generation of biologists has inherited from the leaders of the immediately preceding generation, is the mechanistic one, that life is, in ultimate analysis, a physical and chemical process, and is thus only capable of being understood in terms of the physical and chemical conceptions through which we interpret inorganic phenomena. The second view is that life can only be understood and successfully investigated by means of conceptions derived from the study of life itself. For a recent re-statement of the first view I may perhaps refer to Sir Edward Schäfer's Presidential Address to the British Association in 1912, though I confess at once to standing here as an uncompromising upholder of the second view. According to the first view, biology is only a department of applied physics and chemistry. I wish to claim for biology that "place in the sun" to which it seems to me that she is entitled as an independent science.

The fact of oxygen secretion is one among many facts, all of which tend to show that from the physical and chemical standpoint the functional activities of a living organism are very far from being the comparatively simple processes which they were formerly believed to

be. Orthodox text-books still, it is true, speak of the "mechanism" of such processes as secretion; and the unwary are thus led to believe that these processes are more or less understood as physical and chemical processes. But the blunt truth, enforced again and again by actual investigation, is that if there be any physical or chemical explanation of them, it remains for the present unknown, and with advancing knowledge seems to recede further and further away. This fact is so evident when one looks back over the progress of the last half-century that I need hardly illustrate it. It does not follow, however, that because the supposed physical and chemical processes are too complex for our present powers of analysis, they do not exist. The upholders of the mechanistic theory of life maintain that all the facts hitherto ascertained with regard to the activities of living organisms are simply physical and chemical facts: the movements of living organisms are simply physical movements; and the chemical products of physiological activity are simply ordinary chemical products. For instance, the oxygen liberated in gas-secretion is simply ordinary oxygen, discovered and measured by ordinary chemical and physical methods. When we set ourselves to the task of physiological investigation all we can really do is to investigate the physical causes of the movements and the chemical sources of the products. No other course has any meaning. As a matter of fact, we never actually run up against some mysterious entity, such as the supposed "vital force." We can always push physical and chemical analysis further; and there is nothing for it but to pursue this process from the known and firm

ground of physical and chemical observation into the unknown ground within the living substance we are investigating. The very presupposition of physiology as a science is the assumption that life is a physical and chemical process; and for this reason it is justifiable to speak of the "mechanism" of life, even though we are not yet in a position to understand this mechanism.

Now, it seems to me that this reasoning is radically fallacious; and I shall try to point out the source of fallacy as clearly and shortly as I can. First of all, I wish to emphasise a fact which few biologists seem to realise—namely, that our present interpretation of the inorganic world in terms of such conceptions as mass, movement, atoms, energy, and even space and time themselves, is only an interpretation or working hypothesis. It has been arrived at gradually and laboriously in the course of human history; but we have no reason to suppose that it is a final interpretation, though for the present we cannot dispense with it, and though we can be certain that any truer and deeper interpretations of the physical universe must cover the facts which our present interpretation covers, just as Lavoisier's conception of chemical change covered all the facts interpreted by Stahl's phlogiston theory, to which such able investigators as Priestley and Cavendish held throughout. As a matter of fact, we are living in a time when the ablest mathematicians, physicists and chemists clearly perceive the limitations of the interpretations in which they were brought up, and are striving after deeper and truer interpretations.

To those biologists, therefore, who argue that all the facts which biological investigation reveals are, and can

only be, physical and chemical facts as interpreted in the light of current physics and chemistry, it must be pointed out that they are referring not to bed-rock reality, but to interpretations of that reality; and, moreover, to interpretations which physical science itself is showing to be imperfect, not to mention objections which seem to me of an even more formidable character from the philosophical side.

In the interpretation of Nature we have to look, not merely at the immediate sense data, but at the accompanying phenomena. When a piece of metal burns, the residue is heavier than the original metal. This might be due to the loss from the metal of something with a negative weight, phlogiston, or to gain by the metal of something of a positive weight. It was only by investigating the accompanying phenomena—the disappearance of what we now call free oxygen in the process—that Lavoisier showed the second hypothesis to be better than the first. Now, in the interpretation of the phenomena life we are equally bound to look at the phenomena which accompany each phenomenon which we are investigating; and it is here, as it seems to me, that the mechanistic biology has signally failed. It takes individual physiological data, as interpreted in the light of current physical and chemical theory, and assumes them to represent bed-rock fact. It then endeavours to piece these individual data together, so as to represent an intelligible physico-chemical process; and the result has been failure, which with advancing knowledge seems only to become more and more hopeless.

In investigating a living organism we have no right

to take our data one by one; for, as I shall presently show in more detail, it is characteristic of a living organism that the details of form, movement, chemical composition, and change which we distinguish in it are essentially, and not merely accidentally, connected with one another. We are accustomed to the fact that a limb, or even a bone, of a certain build is associated with a whole body of a certain build. We know also that if an animal is breathing we may expect to find its heart beating and all its other organs in a state of more or less evident activity. We associate together the details of structure and activity as those of a living animal; we think and speak of it as alive, and we regard its structure and activities as the expression or manifestation of its life. What I wish to maintain is that in so regarding a living organism we use a hypothesis which is for biology just as intelligible, just as elementary, just as true to the facts known, and just as good a scientific working hypothesis, as is the hypothesis of the indestructibility of matter for physics and chemistry.

The mechanistic theory of life assumes that in ultimate analysis it is only an accident that material particles of which the living body is composed are aggregated and combined in the form actually met with, and another accident that they display the activities actually observed in the living body. This follows from the conception of organisms as simply material systems in motion or at rest; for the physical world as it is ordinarily conceived consists of matter and energy which are eternal and unchangeable, while of their actual distribution no explanation is given except that it depends on

their previous actual distribution, of which no account is given.

Now let us try to analyse an actual example of physiological investigation. I have sometimes been good-naturedly chaffed by physiological brethren for preaching anti-mechanistic doctrines, and actually employing rigid physical and chemical methods in experimental work, and reaching equally definite physico-chemical results; so I will select for analysis the corner of physiology at which I have mainly worked, namely, the physiology of respiration.[1]

The act of breathing consists of rhythmic muscular movements of the chest-walls, causing the lungs to expand and contract, and air to enter and leave them. These movements of the air are accompanied by chemical changes, oxygen being absorbed from it in the lungs, and carbon dioxide being given off. This is a general statement in physical and chemical terms of the most evident phenomena connected with respiration, and we have now to follow up the physico-chemical analysis. The oxygen which disappears in the lungs passes into the blood through the very delicate epithelium lining the walls of the lung alveoli; and during rest under ordinary physiological conditions the passage inwards has been found to occur in strict accordance with the known laws of physical diffusion of gases. Nearly all of this oxygen then enters into a loose and easily dissociable chemical compound with the hæmoglobin contained in the red blood-corpuscles of the venous blood

[1] The papers published by my pupils and myself on this subject will be mostly found in the *Journal of Physiology* from 1892 onwards.

supplied by the right side of the heart to the lungs. In this form the oxygen is then carried on in the arterialised blood, and is distributed by the action of the left ventricle to the capillary blood-vessels all over the body. In these delicate vessels the partial pressure of oxygen is lowered owing to the passage of oxygen outwards into the living tissues; consequently the oxyhaemoglobin is partly dissociated, so that the red corpuscles deliver up the extra charge of oxygen which they had received in the lungs; and the blood returns through the veins to the heart and lungs, where it receives a fresh charge of oxygen and repeats the cycle.

The carbon dioxide of the expired air is also carried by the blood in easily dissociable chemical combination. It is given up to the lung air by diffusion through the alveolar walls; and the arterial blood returns to the systemic capillaries, where it takes up a fresh charge, owing to the higher partial pressure of carbon dioxide in and around these capillaries. Both the final disappearance of free oxygen, and the production of carbon dioxide, appear to occur within the living cells of the tissues.

The muscular movements associated with respiration are initiated by nerve impulses controlled from a "centre" situated in the medulla oblongata. The rhythmic activity of this centre is influenced by afferent stimuli of different kinds, and by stimuli proceeding from other centres; but all the main control of the centre has been found to depend on the chemical state of the blood supplied to the centre from the heart. Of this latter control we must now consider the nature. We know from the most casual observation that the breath-

ing varies considerably in both depth and frequency, and becomes very irregular during irregular exertions such as speaking or singing. There are many people who think that the lungs may not be getting enough oxygen, and who in order to remedy this imaginary defect recommend increased breathing.[1] Now exact investigation shows that the breathing in each person is so regulated as to maintain during rest a certain absolutely definite mean percentage, or more correctly, partial pressure, of carbon dioxide in the air of the lung alveoli. This percentage depends on the balance between the varying amount of carbon dioxide coming off from the venous blood, and the amount of fresh air introduced into the lung alveoli by the breathing. By an effort of will we can temporarily increase the breathing so as to dilute the carbon dioxide further; but a dilution of as little as one-thirtieth in the mean alveolar carbon dioxide percentage causes the disappearance of all spontaneous impulse to breathe, until the carbon dioxide balance has been restored; while an increase from any cause of one-twentieth in the mean alveolar carbon dioxide percentage is accompanied by an increase to more than double in the volume of air breathed. The average breathing is thus regulated with almost incredible exactitude in accordance with the varying rate at which carbonic dioxide is produced in the body, and brought to the lungs by the blood.

The percentage or partial pressure of carbon dioxide in the alveolar air determines the partial pressure of

[1] By one of Nature's ironies, one effect of forced breathing is to produce dizziness, and even loss of consciousness, due possibly to want of oxygen induced indirectly.

this gas in the arterial blood; and it has been found that it is to this that the activity of the centre responds in regulating the breathing so exactly. Now, carbon dioxide when dissolved in a liquid such as the blood acts as a very weak acid, although its influence as an acid is far less in the blood than in pure water. Careful investigation has shown that the arterial blood is faintly alkaline, and that what the respiratory centre is doing in regulating the partial pressure of carbon dioxide in the blood is in reality to regulate this faint alkalinity. No existing physical or chemical method of demonstrating changes in alkalinity approaches in delicacy the discrimination of the respiratory centre; but by indirect means the proof has been given that the variations in the activity of the centre are caused by minute variations in the alkalinity of the blood.

In the respiratory centre we thus have, to use orthodox mechanistic language, a "mechanism" tuned to react with astounding delicacy and constancy to the minutest changes in the alkalinity of the blood. This supposed mechanism consists of what is called "protoplasm"; and protoplasm is something which from the physical and chemical standpoint is excessively unstable, and sensitive to every slight change in its environment. Yet this unstable mechanism reacts in the human body hour after hour, day after day, year after year, true as tempered steel, to one absolutely definite and absolutely puny stimulus! How can we conceive that such constancy is maintained? Knowing what we do of the nature of living protoplasm, the answer must be that the physiological environment of the respiratory centre remains constant. But how, considering only the vary-

ing quality and amounts of the substances we eat and drink, and which pass through our blood, can this physiological environment be at all constant ? I will leave this question for the moment and meanwhile follow up another path in the analysis.

The actual faint alkalinity of the blood and its power of carrying carbon dioxide in readily dissociable chemical combination depend on the presence in the blood in certain amounts, and in a certain mutual balance, of a number of substances ; and it is clear that, if an alteration in this balance occurred, the degree of alkalinity in both arterial blood and tissues would also be very seriously disturbed unless compensated by considerable variations in the alveolar carbon dioxide percentage and the rate of circulation. Now, during rest under normal conditions of health such variations do not occur to any extent which is appreciable except by unusually exact measurement, or which is more than a very temporary or passing change. Among the many exact regulations which exact quantitative research is rapidly revealing within the living body none is more remarkable than the exactitude with which the capacity of the blood for carrying carbon dioxide is regulated. Such variations as ordinarily occur are within the limits of error of the most exact methods which we have been able to devise for the purpose. The balance can, it is true, be upset temporarily by artificial means ; but in a very short time it rights itself.

The salts of the blood, on which this balance mainly depends, must, in the long run, be regulated by the balance between absorption from the intestine and excretion by the kidneys. So far as we know, all soluble

salts are absorbed more or less quickly by the intestines; and it is therefore to the kidneys that we must mainly look for the explanation of this marvellous regulation of the composition of the blood.

Now, all we know of the mode of action of the kidneys goes to show that they have the same delicate and exact power of regulating the liquid and crystalloid constituent parts of the blood as the respiratory centre possesses in regulating the reaction or hydrogen ion concentration. We actually find that salts and other soluble crystalloids introduced into the body by the mouth or in other ways in excess are promptly excreted by the kidneys. On the other hand, we also find that the kidneys have an equally marked power of holding back substances which are not in excess. If, for instance, a diet free from sodium chloride is given, the chloride in the urine, normally abundant, practically disappears, although there is still nearly the usual high proportion of sodium chloride in the blood-plasma.

Let me give another illustration. We know that when a person who is not thirsty drinks a large amount of water, the consequence is an approximately equal secretion of urine by the kidneys. Further investigation shows that the urine secreted is practically nothing but pure water. When, during the enormous kidney secretion produced by this means, the blood was examined, we found that it was sensibly undiluted by the water passing through it; for the percentage of hæmoglobin in the blood remained sensibly the same during, before, and after the secretion.

Now, it has already been found, through exact observations, that minute alterations in the alkalinity of the

blood provide the stimuli which regulate the varying activity of the respiratory centre, and we never doubted that similar alterations would be found to account for the varying activity of the kidneys, so we sat down to find them. Using another method of attack, my colleague, Dr Priestley, was able to demonstrate that the electric conductivity of the blood was sensibly and regularly, though only very slightly, diminished during the period of increased secretion. It is known that when water is taken into the intestine, not only is water absorbed, but, for a time at least, salts pass out from the blood into the water. Thus one can probably account for a slight deficiency of salts, or "wateriness," in the blood, without any necessary increases in its volume. This deficiency of salts is indicated by the electrical conductivity method, and doubtless produces the stimulus which excites the kidney to increased action.

The conception of the kidney to which modern investigation points is thus that of an organ which responds with almost incredible delicacy to various slight changes in the composition of the blood, and so responds as to keep the blood composition normal. The old gross mechanistic conceptions of fifty years ago with regard to the action of the kidneys are entirely obsolete, though they still occupy a time-honoured place in current text-books. The kidney, if it be a mechanism, is, like the respiratory centre, one of extraordinary delicacy and constancy in action, and we are again up against the question how, with such a labile structure as protoplasm, such constancy can be maintained in the physiological environment of the secreting epithelium as will

correspond to the constancy of action of the supposed secreting mechanism.

Whatever organ in the body we turn to we shall certainly meet with similar delicacy and constancy of reaction when we investigate closely and quantitatively the function of the organ. The blood forms a common internal environment for the living cells of the body, and we know from experiment that the constancy in reaction of the different organs of the body depends upon the constancy in composition of the blood. But evidently this is no explanation, for, as we have already seen, the constancy of the composition of the blood is itself the outcome of the activity of the organs of the constancy of whose reactions we are seeking an explanation. It is only a game of battledore and shuttlecock to attempt to explain one of these facts by the other.

We are thus driven back to the external environment for an explanation; and at first sight this may seem a hopeful direction in which to look. The nutrition of an organism, with all that this implies, depends evidently on the supply of nutriment, water, and oxygen; and it is equally true that the behaviour of the organism depends on the sum of the stimuli acting upon it. We can verify these facts experimentally; and those who uphold the mechanistic theory of life have often pointed to this verification as a justification of their hypothesis. But when we look at the facts a little more closely, and particularly when we investigate them quantitatively, we soon see that we are no further forward. For the organism itself determines the stimuli to which it responds and the ratio between physical stimulus and actual response. Whether food is abundantly available or just

sufficient, it makes little or no difference to the consumption in the long run if that consumption is measured, in terms of energy value; and whether light is superabundant or just sufficient it makes, within enormous limits, equally little difference to our sense of the brightness and visibility of things. It is the same with oxygen. On the summit of Pike's Peak, with the partial pressure of oxygen in the lungs only half the normal, there was not the slightest diminution of the oxygen consumption, just as there is not the slightest increase when pure oxygen is breathed and the partial pressure in the lungs is six times the normal. The organic determination which dominates the internal environment of the body dominates also the causal influence on the body of the external environment. Hence we cannot possibly look to the constancy of physical and chemical influence of the external environment for an explanation of the constancy of the internal environment and activities of the body. We should again be playing an aimless game of battledore and shuttlecock. If we seek for a "causal" explanation in the past history of the organism itself, we are no better off.

The end of the argument is in sight. The phenomena represented by a living organism cannot possibly be grasped and interpreted one by one, in the manner in which we grasp and interpret what present themselves to us as physical or chemical phenomena occurring in space and time. We must grasp them as a whole, simply because, whether we will or not, they present themselves to us as an organically determined whole. If we take them one by one as events in space and time, and let slip our mental grasp of the whole, we find, as I

have already tried to explain in detail, that we are simply passing backwards and forwards in an absolutely helpless and aimless manner.

Someone will perhaps say, I find 200 c.c. measured at 0° C. and 760 mm. barometric pressure of carbon dioxide given off in one minute in the expired air. Is not this a solid, indisputable, and independent fact, whatever be the nature of the organism which expired the carbon dioxide ? The true answer to this question is a blunt and bold negative. The statement about the carbon dioxide is no statement of immediately evident fact, but a highly theoretical interpretation of certain very limited sense data. When we extend our observations we see that what we interpreted at first as a mere flow of gas-molecules is one of the expressions of the life of an organism. The interpretation in terms of the flow of a certain volume or mass of gas molecules was only a preliminary interpretation, satisfactory so far as it went, but also untrue, because it involved a physical interpretation inconsistent, as we have just seen, with the physiological facts taken as a whole. If we start our physiological investigations with such assumptions as that the flow of a certain mass of gas in a certain time is a certain, solid, and independent fact, we are inevitably carried forward by actual investigation up to the point where we finally realise that our interpretation cannot interpret the facts.

We can now get a clearer view of what the true aim of physiology is. We can see, also, that this aim reveals itself to us in actual physiological observation and experiment. In the crude sense-material which presents itself to us we are tracing the thread of constancy in

which the living organism manifests itself; in the apparent chaotic whirl of life-processes we are tracing organic activity. The idea of the maintenance of the faint alkalinity of the blood at once lights up for us and enables us to predict a whole mass of phenomena connected with respiration, circulation and excretion, and points the way to interpretation and treatment of many of the symptoms of disease. Following similar lines, and proceeding always on the assumption that the living organism is really an organism, and no mere machine, physiology can progress steadily and confidently, adding continuously to what is already known about living organisms, and with a clear appreciation of the essential points that await investigation.

No branch of science is in reality more alive and rapidly progressive than the physiology of the present day. Like the bewitched princess, she is waking up to her rightful place, and is meanwhile engaged in brushing away the cobwebs which have been woven round her during her sleep. Among the other cobwebs is the supposition that biology, which deals with what chemists or physicists are apt to look upon as slimy indefinite messes, like blood or protoplasm, is not an exact science. I have already said enough to indicate that in no branch of science are exact quantitative methods and results more essential than in physiology.

The difficulties of a physico-chemical interpretation of life have been felt ever since biology emerged as a branch of science; and I wish now to refer to a hypothesis—that of the so-called "vitalists," by means of which it has been sought to overcome the difficulty. The vitalists are at one with the supporters of the

physico-chemical theory in accepting the physico-chemical interpretation of all the individual facts which we can observe and measure in connection with life; but they also maintain, and very rightly, that the phenomena, taken as a whole, are of such a nature that no merely physico-chemical explanation of them is conceivable. To fill up the gap, they make the assumption that a non-physical influence—the "vital force" of older writers, or the "entelechy" of Driesch and his followers—exercises a guiding influence on the physical and chemical processes occurring within living matter. In Bergson's writings the same ideas take a more subtle philosophical form, and he maintains that we can only grasp the *élan vital* by intuition, while perception limits us to the physico-chemical world.

I think it must already be evident that the doctrine I have been defending is just as inconsistent with vitalism as with the physico-chemical theory of life. The defect of vitalism is that it seeks to set a limit on ordinary physiological investigation, while as a matter of fact the passing of any such limit is only a matter of further investigation. When we discovered the marvellous accuracy with which the respiratory centre governs the lung ventilation so as to maintain with various rates of discharge of CO_2 a certain partial pressure of carbon dioxide in the alveolar air and arterial blood, we might have pointed to this as an instance of the interference of the guiding "entelechy"; and had we been content with relatively inaccurate methods of gas analysis, the varying stimulus which controls the action of the centre might not have been detected. The action of the kidneys in secreting water is another similar example. It is of no

use to suggest to a physiologist that when an Arcella is in difficulties owing to deficiency of oxygen in the water, or a fish is lying helpless on the bottom because it has lost the gas in its swim-bladder, or a mountain climber is in difficulty from deficient oxygen-pressure in the air, the "entelechy" decrees that in order to put things right the ordinary chemical processes in animal protoplasm shall be reversed, and that oxygen shall be liberated from combination instead of entering into or remaining in it. The physiologist will instinctively look for the actual stimulus and its biological interpretation. This is the only right and rational course, justified abundantly by experience. We neither need, nor will have, any ghosts in physiology! The mechanists are right in rejecting vitalism, and the vitalists are also right in rejecting the mechanistic theory; but there is no reason for accepting either theory. What biology requires to do is to go back to ordinary observation, and to realise that the ordinary work-a-day conception of a living organism—the conception which I have already endeavoured to explain and illustrate to you—is the only working hypothesis which will actually work, and is just as necessary in biology as the fundamental conceptions of mathematics, or physics, or chemistry, are in these sciences.

If we are to get a grip of biological fact—the grip which enables us to predict—we must always keep the whole life of the organism in view, whether that organism be a single cell, or a compound organism, or a species. Thus to investigate respiration without keeping in view the circulation, the action of the kidneys, nervous system and other organs, and all that is roughly included in the term "general metabolism," is work which will

probably lead nowhere, because essential points are likely to be neglected at the expense of trivial details. Respiration is only one aspect of a group of phenomena, which can only be grasped as a connected whole if they are not wrongly or superficially grasped. If we could examine a large living animal piece by piece with a high-power microscope, we should see a vast number of cells, but we could probably form no idea of the animal as a whole, and very little idea of the activities of the cells; and if the magnification were increased a thousand-fold more, we should see nothing of the cells, and should only be lost in a bewildering whirl. It is doubtless true in a certain sense that the life of an organism is the "sum" of its activities; but it is equally true that these activities can only be grasped individually as activities of a whole. The true aim of physiology is to grasp them in this sense; and if we accept this, we can see that physiology is making steady and rapid progress. If, on the other hand, we assume the mechanistic or the vitalistic theory of life, we can see no progress whatever towards a successful application of either hypothesis.

This may perhaps seem a strong statement, for have we not acquired a great deal of knowledge which can only be stated in terms of the physics and chemistry of the body? Surely all this is physiological progress. It is physiological progress just in so far as the physical and chemical data can be interpreted in terms of organic activity. As instances of what I mean, I need only refer to such cases as the function of the respiratory movements, or of the digestive ferments, or of those recently discovered and singularly beautiful adjustments by which the partial pressures of both oxygen and carbon

dioxide are steadied during the passage of the blood through the systemic capillaries. The thread of organic determination running through the working of those processes, and the maintenance of the structures associated with them, is the biological thread, and the only thing about them of any interest to a biologist as such.

I have developed my argument against the mechanistic theory from the point of view of the fully developed organism. If we also take into account the phenomena of development and reproduction, the argument becomes still more conclusive. As if to convince us by an ocular demonstration that the organic whole is in the parts, Nature, in the reproduction of an organism, seems deliberately to scrap everything that might be supposed to be mechanism, and then build the whole organism up again out of one small part. A mechanistic theory of heredity is to me, if possible, more unthinkable than a mechanistic theory of the activities of a fully developed organism.

As scientific working hypotheses the mechanistic and vitalistic theories of life are dead, though they will doubtless have to lie in state for many years before the scientific world is convinced that they are dead. They took origin side by side in observation which was not thorough, and in thinking which was not clear. The distinctively biological working hypothesis which is taking their place is in reality nothing new; for even though it has not been clearly expressed, it has subconsciously guided biological investigation and modes of thought and expression. The writings of such a man as Harvey are instinct with it; and it seems to me that it is in the light of the guiding ideas and scientific example of Harvey

the experimental biologist, and not those of either Descartes the mechanist or Stahl the vitalist, that biology will continue to progress.

When we examine biological knowledge we find that, however evident in the gross may be the organic determination manifested in the structure and activities of an organism, this determination does not extend to all the observable details. Whether we observe with the naked eye or with the microscope, we find things, so to speak, in lumps or masses of liquid or gas within which we can perceive no organic determination. We also distinguish in a compound organism the constituent cells, each with a more or less independent life of its own, apart from the common life; and, finally, we have the molecules, each with an apparent existence on its own account. As we pass from the organism outwards into the environment the organic determination seems to fade away altogether.

It is clear, therefore, that the idea of organic determination leaves unexplained a great mass of what we actually perceive in connection with life. It only enables us to interpret, or mentally grasp in such a way that we can predict, part of the phenomena, the part so interpreted being what we recognise as specifically biological. To fill up gaps, we cannot avoid making use of physical and chemical interpretations. Imperfect though these interpretations may be, they are the best we can arrive at for the time.

This may be regarded as a defect in the biological working hypothesis; but what I now wish to point out and very strongly emphasise, is that this defect is common to every hypothesis of whatever kind. We apply our

theories to reality, but reality contains infinitely more than any of our theories will express, and much that is entirely inconsistent with them. All scientific description is just like algebra in this respect. Perhaps nothing is harder than to realise this; and scientific education is sometimes of such a character as to suggest a tacit conspiracy to prevent us from realising it. We are apt to make such assumptions as that there can be no question as to the absolute reality of space and time, or matter and energy; and we are accustomed to gigantic amateur philosophical speculations based on such assumptions. We are prone to think of the doubters as rather ignorant and unpractical persons, who have probably never used a chronometer or theodolite or chemical balance or calorimeter, and have consequently no real idea of the rigid accuracy with which the conceptions of time, space, matter and energy work out in practice, and of how helpless we should be without them. We forget the other side, which is, that it is only in a limited part of our experience that these conceptions help us, and that they are in themselves full of hopeless inconsistencies and difficulties when applied to the total reality of our experience. It is far easier to realise what we think we know than what we are really ignorant of; and it is those who most clearly recognise what we are ignorant of, and who have the faith and courage to do their best to remedy this ignorance, who are the real intellectual leaders.

The hypothesis that living organisms exist as such, and that their structure and activities are the expression of their existence, has the same defects as other scientific working hypotheses. All that I claim for it is that in

the special field of biology it enables us to unify our observations, and to predict, just as the conceptions of mass and energy do in another field. I have tried to show you that this conception is necessary to biologists, though it is also inconsistent with the physico-chemical conception of the universe. The inconsistency exists for the present; but there is no reason why, with the advance of both biology and the physical sciences, a common meeting-ground should not be found. I, for one, believe that it will be found, though I am equally certain that it will never be found through attempts to reduce biological phenomena to physical and chemical phenomena as the latter are generally interpreted at present. I am a firm believer in evolution as a scientific working hypothesis; but to me it seems that in tracing the present into the past we are illuminating the past just as much as the present. If we ever succeed in tracing life back to what we at present regard as inorganic conditions, we shall have altered radically and completely our present ideas of what inorganic conditions are; only then shall we have found that meeting-ground which can never be found so long as our present conceptions of the inorganic world remain.

This brings me to a further point, which I can only briefly touch upon. When we analsye the conception of organism we find that it includes both structure and activity as the expression of organism. Organic structure is structure actively present; and the element of constancy in organic activity is organic structure. Even from the purely physico-chemical standpoint organic structure is nothing but a molecular stream. Inasmuch as the conception of organism expresses observations

relating to the association and maintenance of structure and activity, whereas the conceptions of mass and energy allow of no such expression, biology is on a higher plane of knowledge than physics and chemistry. We see deeper into reality in biology, although our vision is less detailed.

A living organism, as a biologist regards it, excludes all those additional elements in knowledge which we meet with in the conception of personality. The world of personality, when we study it, and consider what it implies, gives us a far deeper view into the nature of reality.[1] We find that it is a world of duty—a world not merely of individual personalities scattered in a mysterious void, but a world which, in the answer to the imperative call of duty, shows itself to be one spiritual world.

The flashes of war have lit up for us this spiritual world. The sense that it is our plighted duty to deal with an infamous disregard of elementary right has sent hundreds of thousands of our best and truest into the fighting line, and is marshalling the whole activities of our nation and its allies in a manner in which they never were marshalled before. We are fighting against powerful and resourceful nations, inspired by patriotic motives as strong as our own; nations which have made contributions to human progress which are perhaps as great and as valuable as any we have made; nations with which those of us who in the past have experienced their hospitality and friendship would be foremost in wishing for honourable peace. Yet we are waging this war in

[1] For further discussion of this subject I may perhaps refer to my book, *Mechanism, Life, and Personality*, 1913

the absolute determination to conquer, cost what it may. For we are fighting, not merely for our own advantage or safety, but for a higher duty; and the faith that this higher duty is a real one, and that in following it we are at one with that spiritual reality which is the only reality, gives us a resolution, a courage and a confidence, which could come from no other source.

What is reality? Does all the ghastly horror of the battlefield, with its engines and organisation of destruction, represent it? That is reality no more than the appearance of the physical universe as interpreted by science is reality. But the dying soldier or sailor who thinks not of himself, but cheerily bids his comrades carry on with their duty, has seen and is one with reality.

The conception of duty itself implies that the spiritual world is a world of imperfection, and yet a world of which the very essence is in the fight with imperfection. We have to tackle the imperfection where we can, and how we can. For this purpose we must study our imperfect world, and act on the best practical knowledge we can get of it. Without the power of predicting the results of our actions we should be helpless. What enables us to predict is science. There is no difference in principle that I can see between the scattered maxims which we call ordinary common sense and the more elementary and far-reaching maxims which we call science. The maxims of common sense vary with the occasions to which they are applicable; but so also do the maxims of science. Common sense prides itself on being practical, and caring nothing for absolute truth, but only for such truth as is practically sufficient for the occasion; whereas each of the sciences, as I remarked at the outset

of this address, is often supposed to express absolute truth. This distinction will not hold. Mathematics confines itself to a world which for the moment may be regarded as empty and void. Physics and chemistry confine themselves to a world which for the moment may be regarded as purely inorganic. It is only for practical purposes that we ever make any of these untrue assumptions; and we only make them because one or other of them is good enough for our immediate purpose, and enables us to act.

This address opened with a question as to what the general aims of scientific endeavour are; and an examination of the aims of biology has led us up to an answer to the wider question as to the aims of science in general. The answer is that scientific generalisations represent, not reality itself, but only certain aspects of it. They are the tools with which we fashion the world of sensuous appearance, and in the fashioning of it reveal its spiritual reality. They are tools of tremendous power, which, if we do not understand and control them rightly, are apt to turn upon and rend us, body and soul; but still only tools, each contrived for limited practical purposes with endless human labour and care, and constantly being increased in efficiency. We who are more immediately concerned in the making of these tools, or who are pioneers or instructors in their use, may often be different persons from the more immediately practical users of them. We may not be manufacturers or engineers, sailors or soldiers, farmers or doctors, lawyers or statesmen; but all are serving the same ends, and all are, or ought to be, concerned in the capacities and limitations of the tools they use. We are not a class aloof

from ordinary affairs, and pursuing far-off truths of no human interest. Our aims and our efforts are no less human, no less practical, and no less worthy, if we pursue them in the right spirit, than those of our sailor and soldier sons, brothers, and countrymen, with whom our hearts now are. We, too, can adopt that splendid motto of the British Navy—"CARRY ON."

III.

THE NEW PHYSIOLOGY.[1]

Looking back on the history of physiology, we can see that there have been various turning-points in general physiological theory, and consequently in the trend of research. Particular discoveries or series of discoveries, often in allied sciences, have led to these turning-points.

The last great turning-point in physiology was about the middle of last century. Up till then it was generally held that in a living organism a specific influence, the so-called "vital force," controls the more intimate and important physiological processes. Inspired by the rapid advances of physics and chemistry, the younger physiologists of that time broke away from vitalism, and maintained that all physiological change is subject to the same physical and chemical laws as in the inorganic world, so that in ultimate analysis biology is only a branch of physics and chemistry.

The subsequent progress of physiology has shown that all, without exception, of the physical and chemical hypotheses then advanced in explanation of intimate physiological processes were far too simple to explain the facts; but the general conclusion that biology is

[1] A lecture delivered before the Harvey Society, New York, October 14, 1916.

only a special application of ordinary physics and chemistry became firmly established, and is still what may be called the orthodox creed of physiologists. It may be truly said that most physiologists look upon this creed as something which has been established for all time, and that they would be inclined to regard any deviation from it as harmful scientific heresy. Nevertheless I think that we have again reached a turning-point, and that a new physiology is arising in place of the physico-chemical physiology which has held sway for so many years. I propose in this lecture to give some account of how, as it seems to me, this new physiology is shaping itself.

It is natural for us to assume that the aim of all investigations in physiology must be to ascertain the causes of physiological activity. However complex a physiological reaction may be, the conditions which determine it can be investigated experimentally; and from long experience we can be quite certain that such experimental investigation will always lead to some result, however obscure. There is, and can be, no limit to experimental investigation of causes. When, however, we examine the results obtained by experimental physiology there emerges a point in which they differ greatly from the results ordinarily obtained in the investigation of inorganic phenomena: for it is characteristic of physiological reactions that they are dependent to an extreme degree on all sorts of environing conditions. We recognise this when we speak of stimulus and response rather than of cause and effect. When the light from a star is focussed on the retina there is a physiological response by night, but none by day. The

response evidently depends on the existing state of excitation of the whole retina. It also depends on the normal nutrition of the retina and brain. If the blood is abnormal in composition, the ordinary response is interfered with ; and we are as yet only at the beginnings of knowledge with regard to the minute changes in blood composition and other conditions of environment which are sufficient to affect the response very materially.

It is the same with every physiological response. The further we investigate the more evident does it become that each physiological response depends on a vast number of conditions in the environment of the responding tissue. On superficial investigation we do not realise this: for we can often get exactly the same response, time after time, with the same stimulus. To the attainment of this result all that is necessary is to see that the conditions are "normal." It is only after more thorough investigation that we find that "normal conditions" imply something which is both extremely definite and endlessly complex. We then begin to realise that the maintenance of normal conditions is from the physical and chemical standpoint a phenomenon before which our wonder can never cease.

Physiological investigation of causes seems, thus, to lead us up to a tangled maze of causal conditions. He who looks for definite "causal chains" in physiological phenomena finds in place of them a network of apparently infinite complexity. The physiologists who led the revolt of last century against vitalism did not see this network. To them it seemed that there were probably simple physical and chemical explanations of the various physical and chemical changes associated

with life. The progress of experimental physiology since that time has effectually shown that this was only a dream, and physiologists are now awakening from the dream.

But we are also awakening from another dream. About the middle of last century it seemed as if, in the current conceptions of matter and energy, we had reached finality as regards the inorganic world. The chemical atom, on the one hand, and the varying energy associated with it, on the other, seemed to represent bedrock reality—a reality including not merely inorganic but also organic phenomena. Discoveries connected more particularly with electrical and electro-chemical phenomena, the periodic law, and radio-activity are awakening us from this dream also. The supposed bed-rock reality of a former generation seems to be melting down before our eyes. The solvent has been the study of particular phenomena, such as those of radio-activity. The professional physicists and chemists have hitherto kept away from the serious study of life. For the most part they have regarded life as something apart, or as a complex physical and chemical phenomenon which is not likely to throw any light on the deeper problems of physics and chemistry. In this attitude I think that they have been mistaken; but in any case it is evident that we must guard against the quite unwarranted assumption that the only possibility of advance in physiology is by the direct application to life of the physical and chemical ideas which held unchallenged sway for so many years.

In this reference I should like to reply to some remarks, made partly with reference to my writings, by my friend

Professor Macallum of Toronto, in a very able and interesting presidential address to the American Society of Biological Chemistry two years ago.[1] After frankly admitting that the apparent difficulties of the mechanistic interpretation of life "put a task upon the human spirit which is apparently not imposed thereon in the theoretic explanation of any other department of science," he proceeds to argue that this is because "our knowledge of the laws that operate in matter is as yet only a very remote approximation to the whole of the lore on this subject that is possibly attainable and that will be ultimately attained." He feels, however, that this defence of the mechanistic theory is somewhat dangerous, and therefore proceeds to point out "that though we know so little of the properties and laws of matter, we know it with a degree of certainty which is not exemplified in the case of any other department of the known or the knowable, and further that the most rational method of interpreting vital phenomena is to explain the unknown in terms of the known, to trace back the causation of the obscure and mysterious to the operations of wholly natural laws and processes."

Now with this latter sentiment I am in entire agreement; but I would point out that Professor Macallum had just invoked, not what he considers the known, but, on the contrary, the totally unknown properties of matter, to furnish us with a future physico-chemical explanation of life. I confess that there is in his argument a certain theological smack which strongly appeals to me as a fellow-Scotchman. In the domain of "apologetics" he would, I feel sure, make a great

[1] *Journal of Biological Chemistry*, xvii. p. viii, 1914.

impression. But in the domain of natural science we have to examine arguments somewhat closely, and it seems to me that his admissions, which are right and unavoidable, carry him so far that his defence of the mechanistic theory of life is wholly unconvincing. One cannot get round the fact that the mechanistic theory has not been a success in the past, and shows no sign of being a success in the future.

When we look broadly at biological phenomena, it is evident that they are distinguished by one universal characteristic. The structure, activity and life-history of an organism tend unmistakably to maintain a normal. Accident may destroy an organism, or even a whole species, but within limits of external environment which are the wider the more highly developed the organism is, the normal life-history of each individual is fulfilled.

If, now, we consider the advance of physiological knowledge from the standpoint of the efforts which have been made, not to ascertain the causes of vital activity, but to track out its normal details, the past history of physiology takes on a new aspect. It becomes a record, not of disheartening repulse before a hopeless wire entanglement, but of continuous progress. The new physiology of which I wish to speak to-night is a physiology which deliberately and consciously pursues this line of progress, leaving on one side what one may call the "causal" physiology handed down to us from the last generation. This new physiology is in one sense not new, but very old. It is only new in the sense of consciously pursuing an aim which has nearly always been instinctively pursued by physiologists, and par-

ticularly by the great physiologist from whom this society takes its name.

Now I think that many of my hearers will at once say that such a course may be useful up to a certain point, but that it is not true science, and that therefore we cannot desert the old attempts. We must, in fact, still continue our frontal attacks on the wire entanglement. To this criticism I shall endeavour to reply later. But meanwhile I should like to explain more clearly, and by means of examples, what the new physiology aims at.

Perhaps I can do this most directly by referring first to the corner of physiology which has largely occupied my own attention—the physiology of breathing.

When we count the breaths, or measure their depth, we find much irregularity, as if there were no very definite or exact regulation of the breathing. Any active occupation, such as speaking or singing, interferes in various ways with the breathing, and the impression at first produced is that the regulation of breathing is very rough. It is also commonly believed that by special training we can increase, or "improve," the ventilation of the lungs. On the other hand, it has been well known for long that the breathing is more or less regulated to correspond with the consumption of oxygen and production of carbon dioxide in the body. Thus during heavy muscular exertion greatly increased breathing accompanies the greatly increased oxidation in the tissues. Another fact well known to physiologists is that if the lung ventilation is by artificial or voluntary means greatly increased for a short time, there follows a period of "apnœa," during which natural breathing

is absent. The exact cause of this apnœa was till recently obscure. In 1868 Hering and Breuer showed that the inflation of the lungs in inspiration gives rise to impulses passing up the vagus nerves, and inhibiting further inspiratory impulses from the respiratory centre, at the same time starting expiration. Deflation of the lungs in expiration has a converse effect. So long as the vagi are intact they are constantly playing this game of battledore and shuttlecock with the respiratory centre, and Hering called this the "self-regulation" (*Selbst steuerung*) of breathing. The apnœa following excessive ventilation of the lungs was interpreted by subsequent physiologists as the summed inhibitory effect of repeated distensions. Fredericq showed, however, that apnœa is produced when the respiratory centre of one animal is supplied with blood from another animal the lungs of which are excessively ventilated. This, therefore, is a true "chemical" apnœa, due to over-aeration of the arterial blood, and was distinguished from "vagus" apnœa. Nevertheless the correlation of the various "factors" apparently involved in the regulation of breathing remained extremely obscure.

I observed that when air breathed is gradually and increasingly vitiated by re-breathing it, or by what is known to miners as "black damp," the breathing is also increased, but not in any simple relation to the extent of the vitiation. With a steady increase in the vitiation the breathing at first increases only a little, but as the vitiation increases further the effect on the breathing is greater and greater. Thus an increase from 4 per cent. to 5 per cent. in the percentage of CO_2 in the inspired air produces about twenty times as

great an effect on the breathing as an increase to 1 per cent. from the normal of 0·03 per cent. Observations of this kind suggested that the breathing is so regulated as to maintain a certain normal percentage of carbon dioxide in the air within the lungs, and that as the percentage in the inspired air rises, a greater and greater increase in the breathing is required to maintain this normal. It is, moreover, excess of carbon dioxide that excites the breathing. A corresponding deficiency of oxygen has no such effect.

It was found by Mr Priestley and myself that a sample of the air in contact with the blood in the lungs could easily be obtained by catching the latter part of the air expired in a deep inspiration. As we expected, the percentage of carbon dioxide in this air turned out to be on an average practically constant for each individual.

If the frequency of breathing is voluntarily varied, even as widely as from three a minute to sixty a minute, the depth adjusts itself so as to keep the average alveolar percentage of carbon dioxide almost absolutely steady; and conversely if the breath is varied. With resistance to breathing there is a similar effect. The effort put into inspiration and expiration is so increased as to overcome the resistance and keep the alveolar carbon dioxide almost steady. If the breathing is temporarily interrupted or abnormally increased, the time is made up afterwards, so that the average alveolar carbon dioxide percentage is practically steady. If, finally, the inspired air is vitiated by carbon dioxide, the breathing is so increased as to keep, if possible, the alveolar percentage approximately steady.

The effects discovered by Hering and Breuer appeared

to them to depend simply on the state of mechanical distension of the lungs, and to have no relation to the chemical regulation of breathing. Mr Mavrogordato and I have quite recently re-investigated these phenomena in man. The results showed that the amounts of inflation or deflation needed to produce the Hering-Breuer effects depend entirely on the chemical stimulus of carbon dioxide. When this stimulus is absent, as in apnœa, a very slight inflation or deflation will suffice, so that the breathing is, as it were, jammed during apnœa; while if the chemical stimulus is strong it needs a great inflation or deflation to produce the Hering-Breuer effect. The vagi prevent useless prolongation of inspiratory or expiratory effort and consequent waste of time in breathing, or damage to the lung structure. They also co-ordinate the discharges of the centre with actual inflations or deflations of the lungs. When the vagi are cut the breathing becomes slow, and, as Scott showed, can only imperfectly respond to an increased chemical stimulus, since the frequency cannot be increased. The influence of the vagi is entirely in the direction of keeping the alveolar air normal. Perhaps nothing illustrates more clearly the dependence of nervous reactions on more fundamental physiological conditions than the varying response of the respiratory centre to the stimulus of inflation or deflation of the lungs.

When excessive ventilation of the lungs is so arranged that there is no fall in the alveolar percentage of carbon dioxide, no apnœa follows. There is thus no such thing as the so-called vagus apnœa. Apnœa is simply due to excessive removal of carbon dioxide from the alveolar air.

When the barometric pressure is varied it becomes evident that the normal which dominates the regulation of breathing is not the percentage of carbon dioxide in the alveolar air, but the partial pressure or molecular concentration. At the normal atmospheric pressure of 30 inches there is about 5·6 per cent. of carbon dioxide in the alveolar air, but only 2·8 at 60 inches barometric pressure, and 1·4 at 120 inches. In these three cases the percentage of CO_2 varies widely, but the partial pressure is the same. It is only with constant barometric pressure that the normal percentage is steady.

When the breathing is increased by excess of CO_2 in the inspired air, or increased production of CO_2 in the body, there is, as might be expected, a slight rise in the alveolar CO_2 percentage. It is this slight rise that is the stimulus to increased breathing. Roughly speaking, a rise of 0·2 per cent. increases the resting breathing by 100 per cent., while a fall of 0·2 per cent. produces apnœa. The stimulus of the increased CO_2 percentage is conveyed to the respiratory centre by the blood. Under ordinary average conditions the centre responds with normal breathing when the blood leaving the lungs is saturated with air containing 5·6 per cent. of CO_2, but does not respond at all when the blood is saturated with 5·4 per cent. of CO_2 or less. The threshold value of CO_2 is, however, greatly lowered by excessive administration of acids or in any condition of so-called acidosis, and is raised by alkalies or an alkaline diet. This and other evidence points to the fact that CO_2 acts on the respiratory centre in virtue of its acid properties when in solution.

According to modern ideas, the acidity or alkalinity

of a liquid depends on its hydrogen ion concentration. The accurate measurement of the hydrogen ion concentration of blood by the electrometric method is attended with great difficulties; but these have been to a large extent overcome by Hasselbalch of Copenhagen, who has obtained measurements of the effects of saturation with different partial pressures of CO_2 on the hydrogen ion concentration of blood. He has also shown experimentally that when the alveolar CO_2 threshold is lowered or raised by an acid or alkaline diet, this raising or lowering is just sufficient to keep the hydrogen ion concentration of the arterial blood sensibly steady. It is now certain, therefore, that what the respiratory centre is reacting to when it reacts to a slight increase in the alveolar CO_2 percentage is the consequent slight increase in the hydrogen ion concentration of the blood.

The latter increase is so minute that it can only be detected electrometrically when it is of sufficient extent to produce very gross changes in the breathing. The respiratory centre is enormously more delicate as an index of change in hydrogen ion concentration of blood than any known physical or chemical reaction.

As already remarked, the alveolar CO_2 percentage is extremely steady under ordinary conditions. This implies that the hydrogen ion concentration of the blood is regulated with almost incredible delicacy, and must be so regulated apart altogether from the breathing. The breathing simply regulates the rapid disturbances in hydrogen ion concentration caused by variations in the production of CO_2: other disturbances are regulated otherwise than by the breathing. There is clear evidence that both the kidneys and the liver play a part in this

regulation; but of the marvellous accuracy of the regulation, physiologists had, till the recent work on the physiology of breathing, no clear conception.

It is not merely the hydrogen ion concentration of the blood that is accurately regulated, but also its capacity for taking up a constant amount of CO_2 in presence of a constant partial pressure of this gas. This capacity depends on the concentration of and balance between alkaline salts and albuminous substances in the blood. Recent investigations by Christiansen, Douglas and myself have shown that this concentration and balance are so accurately maintained day by day, and month by month, that, under normal conditions, no deviations can be detected by the most delicate existing method of blood gas analysis. The balance can be temporarily upset by what may be called violent means; but within an hour it is back again to normal. It is, of course, evident that if the carrying-power of blood for CO_2 did not remain normal, the breathing and circulation would not, without special adjustment, remain normal.

Now let us look back for a moment, and see where we stand. The experimental study of the physiology of breathing has led us to the discovery of four normals, the maintenance of which furnishes the interpretation of a mass of what would otherwise be isolated and unintelligible observations. We have first of all the normal alveolar CO_2 pressure. This turns out to be directly subordinate to the normal regulation of the hydrogen ion concentration of the blood, the normal reaction of the respiratory centre to hydrogen ion concentration, and the normal regulation of the capacity of the blood for carrying CO_2. With the discovery of each of these

normals we have obtained deeper and deeper insight into the physiology of breathing. We have done this, not by merely seeking for causes in the physical sense, but by seeking for interconnected normals and their organisation with reference to one another and to other organic normals. These normals represent, not structure in the ordinary physical sense, but the active maintenance of composition. We may fitly call this living structure, since so far as we know all living structure is actively maintained composition, the atoms and molecules entering into which are never the same from moment to moment, according to the physical and chemical interpretation. Our method has thus been essentially the same as that of the anatomist who seeks for the normal—the type—which runs through and dominates the variety of detail which he meets with, and who reaches more and more fundamental types.

I wish, now, to point out that the same method has been applied, and is being applied, to other departments of physiology, even though the physiologists applying it may have failed to realise the far-reaching significance of their results.

I will refer first to the general physiology of the blood. The facts that the hydrogen ion concentration and capacity for carrying CO_2 are very accurately regulated in the blood are no isolated facts in physiology, although the accuracy of our physiological means of measurement renders them peculiarly striking. Claude Bernard, in his *Leçons sur les phénomènes de la vie*, was, I think, the first to point out clearly that the composition of the blood, as well as its temperature, is physiologically regulated. He was led to this conclusion more particularly

by his observations that in prolonged starvation there is still sugar in the blood, and that even when great excess of sugar is introduced into the body the percentage in the blood remains very steady, as excess is taken up by the liver and other organs, or excreted by the kidneys. Voit's observations on the relative constancy of the sodium chloride in the blood, and the manner in which the kidneys regulate this percentage, are of a similar character. If food freed from chloride is administered, the elimination of chloride by the urine diminishes to almost nothing, though the high percentage of chloride in the blood-plasma remains about the same. As Voit also showed, the blood during prolonged starvation retains its normal composition, and its volume remains proportional to body weight, while other tissues (*e.g.*, muscle) are disproportionately reduced.

Dr Priestley and I have recently investigated the excretion of water by the kidneys. By simply drinking large quantities of water one can produce an enormous increase in the secretion of urine, and this urine is almost pure water. What we wished to observe was the degree of watering down of the blood which was necessary to produce the huge increase in excretion of water. We did not doubt that the watering down would be very small, but when we attempted to measure the dilution by determining the percentage of hæmoglobin, we found that there was no dilution at all, though the method used was one of extreme accuracy. When, however, the plan of measuring the electrical conductivity of the serum was adopted, a slight, but quite distinct, diminution in the conductivity could be detected during, and ending with, the diuresis. This showed that there was a slight diminu-

tion in the salt-concentration, to the effects of which the secreting cells were reacting. Here, then, we are in presence of another exactly but elastically regulated normal, the slightest deviation from which produces, in the kidneys, a reaction comparable in its exquisite delicacy with the reaction of the respiratory centre or liver or kidneys to a change in hydrogen ion concentration.

The physiology of the kidneys has, in accordance with prevalent physiological conceptions, been attacked from the side of "causal" explanation. I know nothing more hopeless than the attempts to explain the outstanding features of secretion of urine on the lines of ordinary physics and chemistry. So far as the facts are yet known, we can, however, get a practical grasp of the kidney activities if we attack the subject from the standpoint of the active maintenance of the normal blood composition.

Let me turn now to the general physiology of nutrition. In the preliminary stages of investigation of this subject physiology has owed much to the pure chemists, and this debt is constantly increasing. We have only to think of the work of such men as Black, Priestley, Lavoisier, and Liebig. Like Wöhler, who synthesised urea, Liebig was a convinced vitalist. For him there was a central kernel of vital activity under the control of the "vital force"; but outside this central kernel he interpreted the phenomena of nutrition on purely chemical lines. He thought of oxygen as something free to oxidise anything oxidisable within the body, except what is protected by the vital force; and he assumed that the greater the concentration of oxygen in the lungs, and the greater the supply of food-material to the body, the greater will

be the amount of oxidation, since only a limited amount of oxidation is under the direct control of the vital force. He gave special attention to the elimination of urea and other products of nitrogenous oxidation, and introduced methods of measuring the nitrogenous waste. It was found, apparently in direct confirmation of his general ideas, that the amount of urea excreted rises and falls, except for a certain starvation minimum, in direct proportion to the amount of albuminous food eaten. The excess over the starvation minimum was looked upon as "luxus consumption"—an ungoverned oxidation due to simple chemical factors.

But the matter was soon carried further by the physiologists—particularly by Pflüger, and by Voit and his pupil Rubner. It was found that, other conditions being equal, the consumption of oxygen is within wide limits independent of the abundance of its supply, and that the actual consumption of oxygen per unit of body weight is very little different during starvation from what it is when abundant food is supplied. In starvation more fat is being oxidised to compensate for the deficiency in albuminous oxidation. Finally, the brilliant work of Rubner established the fundamental fact that within very wide limits different food substances are simply substituted for one another within the organism in direct and exact proportion to the energy which they furnish when broken down. The energy liberation per unit body weight is practically constant, but if excess of food is taken, the excess of potential energy is stored up as fat and glycogen, while if food is withheld, the stored excess is used up. Even when all the stored fat and glycogen is used up, the organism finally flings its own

living structural substance into the balance, and in this last desperate effort to maintain the normal metabolism the nitrogenous oxidation again rises to an amount which for a short time compensates for the energy previously yielded by fat. When death from starvation at length comes, the old flag—the flag of life—is still flying.

The massive work of Atwater and his pupils on human nutrition, in which it was shown that the normal daily food requirement of a man is about 3500 calories in energy value, was of course a direct extension of the idea of normal nutrition. We maintain an energy consumption of about 3500 calories, just as we maintain about 5·6 per cent. of CO_2 in our alveolar air, or hæmoglobin of 18·5 per cent. oxygen capacity in our blood, or legs of a certain length and anatomical structure. By a strange confusion of ideas, the idea is abroad that nutrition is a matter of simple chemistry and physics, and that when we estimate food values in calories, we are exemplifying this fact. This is enough to make staunch old vitalists like Harvey or Johannes Müller turn round in their graves and laugh. What is it in the body that measures out or withdraws protein, carbohydrate and fat with meticulous accuracy in terms of their energy value, in such amount as to maintain the normal energy metabolism ? Is it not the vital spirit or vital force ? the old physiologists would ask. Is not this phenomena of a piece with all the other distinctive phenomena of life, and ought not physiology to face these phenomena fairly and squarely and generalise from them, not run away from them ? This is the question I am trying to put to you now.

Now I wish to make it clear that it is not vitalism,

but simply biology, that I am preaching. Vitalism is a very roundabout and imperfect attempt to represent the facts. Physiological study, and biological study generally, seems to me to make it clear that throughout all the detail of physiological " reaction " and anatomical " structure " we can discern the maintenance of an articulated or organised normal. This idea brings unity and light into every corner of physiology. In other words, it helps us within limits to predict, just as the ideas of unalterable mass and energy help us within limits to predict, or the ideas of time and space help us within limits to predict. I claim nothing more for it, but also nothing less. The idea of life is just the idea of life. One cannot define it in terms of anything simpler, just as one cannot define mass or energy in terms of anything simpler. But this one can say—that each phenomenon of life, whether manifested in " structure," or in " environment," or in " activity," is a function of its relation to all the other phenomena, the relation being more immediate to some, and less so to others. Life is a whole which determines its parts. They exist only as parts of the whole.

At first sight it seems as if it must be very difficult to make use of this conception as an instrument of research: for evidently we cannot investigate the parts without investigating the whole. The difficulty is only apparent. The whole is there, however little we as yet comprehend it. We can safely assume its presence and proceed to discover its living details piece by piece, in so doing adding to our knowledge of the whole. If, on the other hand, we attempt to take the organism to pieces, or separate it from its environment, either in

thought or in deed, it simply disappears from our mental vision. A living organism made up of matter and energy is like matter and energy made up of pure time and space : it conveys to us no meaning which we can make use of in interpreting the facts.

But is there not matter and energy in a living organism ? Do we not assume this at every step in physiology? We make use of the ideas of matter and energy in biology, just as the physicist makes use of the idea of extension in the investigation of matter. To the biologist, however, the structure and activity of an organism are no mere physical structure and activity, but manifestations of life, just as to the physicist the extension of matter is no mere mathematical extension, but a manifestation of the properties of matter, with a physical and not a mere mathematical meaning. This is the answer to those who point to the dependence of physiology on physics and chemistry, and conclude from this that physiology cannot be anything but a department of physics and chemistry. By a similar chain of reasoning physics would be nothing but a branch of mathematics, and mathematics itself would melt away into that universe of unconnected "impressions" which David Hume imagined, but Immanuel Kant showed to be non-existent.

The limits of time prevent my giving further examples of the light which the conception of the normal throws on the details of every part of physiology, and I must now try to probe more deeply. It may be pointed out that although it is useful in matters of detail to bear in mind that a living organism tends to maintain a normal of both structure and activity, and to pass through a

normal life-history, yet in ultimate analysis all this *must* be due simply to the reactions between its physico-chemical structure and environment. I will not at this point quarrel on general grounds with the "must," but simply endeavour to test it by the facts of physiology.

We can distinguish in a living organism what seems a more or less definite structure of bony matter and connective tissue. Yet we know that all this is built up, and in adult life is constantly being pulled down, rebuilt and repaired, through the activities of living cells. It is thus within the living cells that we must look for the structure which is supposed to react so as to maintain the normal. These cells are made up of what has been called "protoplasm." Now the more we study protoplasm the more evident does it become that this "substance" is extraordinarily sensitive to the minutest changes in environment. Take away or diminish or increase the minute traces of calcium or potassium salts in the blood-plasma, or the traces of various substances supplied to the body by other organs; or add traces of certain other substances: the reactions of the protoplasm are quickly altered, and its structure may be destroyed. It is evidently in active relation with its environment at every point, and one cannot suspend this activity without altering it. Even deprivation of oxygen for perhaps a minute may kill a nerve-cell. There is no permanent physical structure in the cell: the apparent structure is nothing but a molecular flux, dependent from moment to moment on the environment.

Now, when we look at the blood, the internal or immediate environment on one side of the cells in the body, we find, as already shown, that this is almost incredibly

constant in composition. Were it not so the reactions of the cells would become chaotic, and their structure would be completely altered, if not destroyed. But the constancy of the blood is maintained by the combined reactions of the organs and tissues themselves. The intimate structure of the living cells depends on the constancy of the blood, and the constancy of the blood depends on the intimate structure of the tissues. If we regard this condition as simply a physical and chemical state of dynamic balance, it is evident that the balance must be inconceivably complicated, and at the same time totally unstable. If at any one point in the system the balance is disturbed, it will break down, and everything will go from bad to worse.

A living organism does not behave in this way: for its balance is active, elastic, and therefore very stable. When a disturbance affects its structure or internal environment, it tends to "adapt" itself to the disturbance. That is to say, its reactions become modified in such a manner that the normal is in essential points maintained. An injury heals up: destroyed tissue is reproduced, or other parts take on its function: the attacks of micro-organisms are not only repelled, but immunity to future attacks is produced. In reproduction the body periodically proceeds to renew almost the whole of its structure. Death may be regarded as a periodical scrapping of structural machinery, and reproduction as its complete renewal.

The Anglo-American expedition of which I was a member studied, on the summit of Pike's Peak, Colorado, adaptation to the want of oxygen which causes, in unadapted persons, all the formidable symptoms known

as "mountain sickness." As adaptation proceeded, the blueness of the lips, nausea, and headache completely disappeared, and it was then found that even during rest the lung epithelium had begun to secrete oxygen actively inwards. The kidneys and liver were now also regulating to a lower degree of alkalinity in the blood, so that the alveolar CO_2 pressure was diminished, and the breathing consequently increased, thus raising the oxygen-supply to the lungs. There was also a marked increase in the hæmoglobin percentage and in the blood volume. The organism had so adapted itself as nearly to compensate for the deficiency in oxygen-supply, just as a heart gradually compensates for a permanent valvular defect.

The normals of a living organism are no mere accidents of physical structure. They persist and endure, and they are just the expression of what the organism is. By investigation we find out what they are, and how they are related to one another; and the ground axiom of biology is that they hang together and actively persist as a whole, whether they are normals of structure, activity, environment, or life-history. In other words, organisms are just organisms, and life is just life, as it has always seemed to the ordinary man to be. Life as such is a reality. Physiology is therefore a biological science, and the only possible physiology is biological physiology. The new physiology is biological physiology—not bio-physics or bio-chemistry. The attempt to analyse living organisms into physical and chemical mechanism is probably the most colossal failure in the whole history of modern science. It is a failure, not, as its present defenders suggest, because the facts we

know are so few, but because the facts we already know are inconsistent with the mechanistic theory. If it is defended, it can only be on the metaphysical ground that in our present interpretation of the inorganic world we have reached finality and certainty, and that we are therefore bound to go on endeavouring to interpret biological phenomena in the light of this final certainty. This is thoroughly bad metaphysics, and equally bad science. It is the idea of causation itself that has failed, and failed because it does not take us far enough. We have not at present the data required in order to connect physical and chemical with biological interpretations of our observations; but perhaps the time is not far off when biological interpretations will be extended into what we at present look upon as the inorganic world. Progress seems possible in this direction, but not in the direction of extending to life our present every-day causal conceptions of the inorganic world.

I now wish to add a few words as to the relation of physiology to medicine; for I am one of those with an intense belief in the intimate connection between the two subjects, and it seems to me that the mechanistic physiology of the nineteenth century has failed to take the rightful position of physiology in relation to medicine. What is the practical object of medicine? It is to promote the maintenance and assist in the re-establishment of health. But what is health? Surely it is what is normal for an organism. By "normal" is meant, not what is the average, but what is normal in the biological sense—the condition in which the organism is maintaining in integrity all the

interconnected normals which, as I have already tried to indicate, manifest themselves in both bodily structure and bodily activity.

Now, for the mechanistic physiology there are no interconnected normals, just as in the inorganic world as at present interpreted there are also no interconnected normals. If we look through an average existing text-book of physiology, we find a great deal about the effects of this or that stimulus, a great deal also about the external mechanism and chemistry of bodily activity—a great deal, in other words, about what lies on the surface, but never takes us further. Along with this there are perhaps also some inconclusive discussions of the possible mechanism of such processes as physiological oxidation, secretion, growth, muscular contraction, or nervous activity. Very little will, however, be found about what in reality lies still more on the surface, but also penetrates deep down—the maintenance within and around the body of normal organised structure and activity. The maintenance of the normal is something for which there is no place in the mechanistic physiology, since according to this physiology maintenance must be in ultimate analysis only an accident of structure and environment—a fitful will-o'-the-wisp, which does not concern true science.

But medicine, as we have seen, is supremely interested in the physiological normal. What a man sees at the bedside is a perversion of the normal, and Nature's attempts to restore it, with what assistance medicine can give. For medicine it is necessary to know the normal in its elastic and active organisation. He who knows how the body regulates its normal temperature

will not confuse heat-stroke with fever, or make the mistake of attributing fever to mere increased heat-production in the body. He who knows how the breathing is normally regulated will be in a position to distinguish at once between various causes of abnormal breathing; and similarly for every abnormal symptom met with in disease. But the mechanistic physiology gives a minimum of information about the maintenance of the normal. One looks in vain in physiological text-books for connected accounts of the regulation of breathing, circulation, kidney activity, general metabolism, nervous activity. The main facts of physiology are partly ignored, and partly strewn about in hopeless disconnection and confusion. A student of medicine may learn some true physiology at the bedside, or he may never learn it at all, and become either a hopeless empiric or what I do not hesitate to call a mechanistic pedant.

Medicine needs a new physiology which will teach what health really means, and how it maintains itself under the ordinarily varying conditions of environment. We also need a pathology which will teach how health tends to reassert itself under totally abnormal conditions, and a pharmacology which will teach us, not merely the "actions" of drugs, but how drugs can be used rationally to aid the body in the maintenance and re-establishment of health. The new physiology, new pathology, and new pharmacology are growing up around us just now. I can see them more particularly in the splendid advances which the medical and other biological sciences are making in America. You have the advantage of having less of old intellectual machinery to scrap than we have in the old countries; but perhaps we shall not be much behindhand.

If we look on pathology as simply the description of damage to bodily structure, and the analysis of the causes of this damage, then pathology may be very helpful in preventive medicine, but does not help much in therapeutics. When, however, pathology studies the processes of adaptation to the unusual, defence of the organism against the unusual, and reproduction of the normal, just as the new physiology studies the maintenance of the normal under ordinary conditions, then therapeutics and surgery will be aided at every step by pathology, and a rational biological pharmacology will have its chance.

Sometimes one hears the complaint that the world has grown old : that the great discoveries have all been made ; and that nothing is left to us now but to work out matters of sheer detail. Perhaps the great and constantly growing mass of rather uninteresting, but otherwise apparently meritorious, scientific literature increases this impression. At certain moments one may long for the past centuries when there was much less to read, and people seemed to have plenty of time to think, and to have endless material for new discoveries and projects. But in reality I do not think that there was ever more scope for new ideas and discoveries than there is at present. Among the new ideas are those of the new physiology, the outlines of which I have tried to trace in this lecture. Those who do not feel inclined to accept this new physiology, or who are still sceptical as to its theoretical basis, will, I hope, at least make allowance for any personal failure on my part to present it to them in a more convincing form.

IV.

THE RELATION OF PHYSIOLOGY TO MEDICINE.[1]

In spite of the great and striking development of physiology, and of the teaching of it, particularly on the practical side, there is a considerable, and in some respects growing, want of contact between physiology and practical medicine and surgery. As Professor Frederic Lee of Columbia University put it in a recent paper (*Journ. Amer. Med. Assoc.*, vol. lxvi. p. 640): "During their first or second year, or in both, the students receive their instruction in physiology. Most of them follow the course willingly because they have faith in the wisdom of the men who have planned the course, and faith that in some way not now clearly comprehended their training in it will be useful to them later. Nevertheless, too many students question the good judgment that imposes on them a difficult topic, the relation of which to the treatment of sick persons they do not understand. By the end of their second year they have completed their work in physiology, and lay the subject aside with a feeling of relief as they turn to the more congenial occupations of their two clinical years. Now they acquire a new vocabulary for which all along they

[1] Paper read at a meeting of the Edinburgh Pathological Club, January 1918.

have been longing. . . . With the passing of the physiologic words go also their meanings, and throughout the rest of the school career, and too often the rest of professional life, physiology is merely a scientific curiosity."

I wish to make some suggestions as to the causes of, and remedy for, the defects in living contact of physiology and the other immediately preparatory branches of medical study with practical medicine and surgery. I do not think that the causes lie so much on the surface as might at first be supposed. We have, I think, to dig rather deep to discover them, and to dig into a controversial subject. Hence I can hardly look for general assent to my conclusions. I hope, nevertheless, that they may at least give rise to a fruitful discussion.

The aim which medicine and surgery have constantly before them is to help in restoring health and preventing ill-health. Now let us first try to see from actual examples how medical and surgical interference can contribute in this direction. Though I have been outside ordinary medical practice ever since I was house-physician at the Edinburgh Royal Infirmary, my work has kept me in contact with many problems of preventive medicine; and recently the war has brought me, like most other physiologists, back to ordinary problems of practical medicine. I will, therefore, take as examples one or two medical problems with which I have recently been in contact.

The first of these relates to the treatment of the acute stages of poisoning by ordinary lung-irritant gases, such as chlorine, phosgene, or trichlor-methyl-chloroformate. Some hours after a serious exposure to one

of these gases, the soldier begins to present very dangerous symptoms. The colour of the lips and face becomes either blue or leaden coloured : the pulse is rapid, and may be feeble and irregular : the breathing is increased, and a watery sputum is coughed up. At the same time the senses become dulled, and coma may supervene.

What is the meaning of this symptom-complex? Let us begin with the colour of the lips and skin. Evidently the blood in them has no longer its ordinary scarlet colour. This might be due to decomposition of the hæmoglobin by the poisonous gas, with formation of methæmoglobin or other decomposition products. But we can negative this theory very quickly by taking a drop of the blood, diluting it with water, saturating with carbon monoxide or coal-gas, and comparing the tint of the solution with that of normal blood similarly treated. The hæmoglobin shows no trace of decomposition; and if it had occurred, the colour of the lips would have changed immediately after the exposure to the gas, and not many hours later. The colour of the lips is therefore due to the presence of reduced hæmoglobin, as in any ordinary true cyanosis.

This cyanosis might be due either to great slowing of the circulation, or to deficient oxygenation of the blood in the lungs. There is, however, usually no sign of the cold skin and other evidences of great slowing of circulation; and in many cases the blood-pressure is still high, along with great cyanosis. It is evident, therefore, that the main cause of the cyanosis is deficient oxygenation in the lungs, and this in spite of vigorous and rapid breathing, which is evidently not prevented by contraction of bronchi. The cause of this deficient oxygenation

is made evident by post-mortem examination of similar fatal cases, as well as by the character of the sputum. The lung alveoli contain large quantities of albuminous liquid, and the alveolar tissues are swollen and proliferating. The diagnosis is completed by the observation that on administration of oxygen the cyanosis clears up and the circulatory and other symptoms improve. By administering oxygen we largely increase the percentage of oxygen in the lung alveoli, and thereby increase in still larger proportion the diffusion pressure of oxygen into the blood. Under normal conditions the partial pressure of oxygen is about 6 per cent. of an atmosphere in human venous blood, and 13 per cent. in the alveolar air, the difference being therefore 7 per cent. With the presence of liquid and swelling of the alveolar epithelium, the pressure difference present is not sufficient to drive enough oxygen through to oxygenate the blood at all completely. But we can increase the normal pressure difference as much as ten or twelve times by giving oxygen, so that the oxygen goes in far faster; and usually a quite moderate increase in the oxygen percentage of the air suffices to remove the cyanosis. The increase in the breathing multiplies by several times the pressure difference which enables CO_2 to pass out, so that escape of CO_2 is already provided for.

What, now, are the effects of the want of oxygen indicated by the cyanosis? We can observe some of these effects in mountain sickness, where the want of oxygen, to which, without the smallest shadow of doubt, mountain sickness is due, is produced by deficiency in the oxygen pressure of the air. In this case the want of oxygen is slight, but the nausea, headache,

and extreme depression which result after a few hours' exposure to the rarefied air are formidable enough symptoms. Similar symptoms result from slight CO poisoning. With more serious want of oxygen, as in severe and prolonged exposure to CO, or to air very deficient in oxygen, the effects are far more formidable. There is very serious damage to the central nervous system, and both capillary hæmorrhages and large hæmorrhages may occur in the brain. The heart becomes weak and dilated, with the mitral valve probably incompetent. The kidneys and other organs may also be injured; and recovery, if it occurs, is slow and gradual. Evidently, therefore, any serious want of oxygen, if allowed to go on, is a source of great danger, unless the patient has been gradually acclimatised to it, as in some cardiac cases. The breathing, though it is increased, gives no definite warning of this danger. There is, for instance, no marked struggle for breath when a man loses consciousness from CO poisoning or an airman flies to a dangerous height. In phosgene poisoning there is usually no great struggling for breath, as the CO_2, which stimulates the respiratory centre, can easily be got rid of in the lungs.

We can now see that the patient is in the gravest danger and constantly going down the hill from the cumulative effects of want of oxygen, but we cannot undo the damage done to the exquisitely delicate alveolar tissue; much less can we replace it. We know, however, that if we can keep the patient alive, by obviating secondary dangers, the lung epithelium will of itself return to normal or something like normal. Now it is evident that by the continuous administration of

air rich in oxygen we can meet the pressing danger and progressive damage from want of oxygen. To make this administration practically possible it is necessary to have proper apparatus, and I recently devised an apparatus for the continuous administration of oxygen, so that not more is given than is actually required, and none is wasted. This apparatus is in successful use in the clearing stations of our army, and I hope that apparatus of a similar or superior type may soon be applied in ordinary medical practice for use in the numerous cases where oxygen is, so far as I can judge, required.

By giving oxygen we do not cure the lung inflammation. It might, therefore, be objected that in the long run oxygen is useless, and only prolongs suffering. I wish to emphasise very strongly that reasoning of this kind is radically fallacious, and strikes at the root of practically all medical and surgical interference. What we do by giving oxygen is to keep the patient alive, by preventing secondary injury, until time has been given for the natural processes of recovery of the lung. We are breaking a vicious circle, for the want of oxygen produced by the injury to the lung is hindering, or making completely impossible, recovery from the injury. When the want of oxygen is removed, recovery can take place in a normal manner.

Medical or surgical interference of almost any kind amounts to the same thing. By treating a wound antiseptically or aseptically the surgeon breaks another actual or potential circle; for it is the infection rendered possible by the wound that prevents the wound from healing. The natural healing process is free to go on

when infection is got rid of. By the use of anæsthetics another potential vicious circle is broken; and similarly by the use of splints, of operative interference, or simple rest. It is exactly the same with regard to the use of all varieties of drugs. With digitalis or strophanthus, combined with rest, we can often break a vicious circle in heart disease; with drastic measures for reducing body temperature we break a direct vicious circle in heat-stroke. When the vicious circle is broken, Nature is enabled to re-assert herself. Normal regulation of the circulation returns in valvular disease; and the normal physiological control of body temperature is recovered in heat-stroke. But at the back of all medicine and surgery is the old-fashioned *vis medicatrix naturæ*. Without this there would be no such thing as medicine and surgery. We cannot repair the living body as we repair a table or a clock. The surgeon is not a carpenter, nor the physician a mechanician or chemist.

Medicine and surgery are always counting on, and trying to understand and aid, the *vis medicatrix*: they evidently cannot get on without it. Here I think we touch the subtle barrier which causes the estrangement between practical medicine and the teaching of the preliminary sciences; for these sciences, as ordinarily taught, pay little or no attention to anything corresponding to the *vis medicatrix*.

Now let us try to analyse a little more closely what is wrong in the gas-poisoning case. The patient is in urgent danger from want of oxygen. But if we measure his actual intake of oxygen we shall probably find that, owing to his restless condition, it is above, rather than

below, what is usual for a man lying in bed and without food. He is only short of oxygen in the sense that the partial pressure of oxygen in the blood of his systemic capillaries is too low for the proper support of life, though there is still much oxygen left in even the venous blood. When he was still moving about, just before being put to bed or laid on a stretcher, his oxygen intake was far above that of a resting man. Yet probably his lips were already blue, and he was in imminent danger of sudden death from shortage of oxygen. This shows clearly that not only must the blood supply an amount of oxygen proportionate to the very fluctuating demands at different times, but the oxygen must at the same time be distributed at a certain partial pressure or concentration. When we measure the oxygen pressure of the venous blood in a normal person it is extraordinarily steady, in spite of considerable variations in its rate of consumption. This relatively steady normal is no longer maintained in the patient, and his symptoms of oxygen-want are due, not to an abnormally low rate of intake of oxygen, but to a failure in regulation of the manner in which the oxygen is distributed. The truth is that in a normal person the oxygen supply to the tissues is, like everything else in the living body, regulated minutely from minute to minute. To the *vis medicatrix* of the sick body there thus corresponds a *vis directrix* in the healthy body; and just as the *vis medicatrix* restores both structure and function in the sick body, so the *vis directrix* regulates at every moment the activities of the healthy body. The *vis medicatrix* and *vis directrix* are evidently one thing.

This is an old-fashioned and very gross method of

expression, but it at least points to the great salient facts which distinguish an organism from such machines as we know, and completely differentiate medicine from all mechanical and chemical arts. To put the matter in simpler and less misleading language, it is organic regulation of both structure and activity that we are constantly trying to aid and supplement in medicine and surgery.

I do not wish to go into the question whether organic regulation is, or is not, ultimately reducible to mechanism. On this point I have fully expressed my own conclusions elsewhere, but they need not directly affect the matter we are now discussing. My immediate point is this: that in practical medicine the assumption of the existence of organic regulation of both structure and function is absolutely fundamental. Disease is the breakdown of this regulation at one point or another; and practical medicine is simply assistance to Nature in restoring and maintaining effective organic regulation.

Now let us turn to physiology as it is usually taught at present. On consulting a current text-book of physiology one finds an account of the mechanical and physical aspects of each bodily process taken separately. For instance, in the case of breathing, there are descriptions of the structure of the lungs, the mechanism by which air is driven in and out of the lungs, the chemical changes in the air breathed, the means by which gaseous exchange occurs in the lung alveoli, the nervous channels by which inspiratory and expiratory impulses are conveyed from the respiratory centre to the muscles, and the chemical and nervous stimuli which act on the centre. All these things are systematically described one by one, as we

might describe the structure and action of a machine. But there is something which is almost totally lacking, for there is no description of the organic regulation which absolutely dominates all the mechanical and chemical details.

When, for instance, we examine the pumping movements of the respiratory muscles, we find that they are determined by what is required to maintain at a practically constant partial pressure the carbon dioxide and oxygen in the arterial blood leaving the lungs. If the carbon dioxide production and oxygen consumption are increased ten times, the ventilation of the lungs will also be increased nearly ten times, so as to prevent more than a very slight increase in the carbon dioxide pressure of the blood. If the carbon dioxide percentage in the inspired air increases, there is a corresponding result. If the oxygen pressure in the arterial blood tends to fall, it is kept up partly by increased breathing and partly by active secretion of oxygen inwards by the lung epithelium. Failure in these regulative activities produces urgent and dangerous symptoms.

Here, therefore, we have constant, unmistakable, and exact regulation of the quality of the arterial blood by the breathing, and if we examine the structure of the lungs and the nutritive process by which this structure is maintained, the constant teleological regulation or maintenance of structure is no less evident. Now the very expression " teleological regulation " evokes at once emphatic repudiation from most physiologists, as they consider that it savours of mouldy metaphysics. Let us, they argue, keep to facts capable of definite experimental verification, and avoid all doubtful interpretations

of them. This, for instance, is what Huxley expressly aimed at in his admirably written *Elementary Physiology*.

Now I entirely agree with this contention; but the question remains as to what *are* the facts. It seems to me that, quite unconsciously, Huxley, and the whole physiological school which he typifies, misrepresented them very seriously, and in the manner which is really responsible for the existing and very detrimental estrangement between practical medicine and the preliminary medical sciences. It is quite evident that the breathing is regulated in the manner just described. One can verify it with the greatest ease. But if we teach physiology as if it dealt with a series of essentially unconnected events, like the workings of the separate parts of a machine, we misrepresent the facts.

We know, for instance, that under ordinary conditions the presence of a certain very minute excess or deficiency in the pressure of carbon dioxide in the alveolar air will cause great increase in the breathing, or bring natural breathing to a complete standstill. This seems simple and definite; but as soon as we alter the conditions by diminishing the normal pressure of oxygen in the air, or interfering with the circulation, or overdriving the muscles, or making the diet abnormal in certain directions, or in various other ways altering the "normal" conditions, the statement is no longer true. The definite effect of the CO_2 is no longer the same. The effect depends very directly on the normal functioning of the body as a whole, and its immediate environment; and when we consider the alteration in the effect we find that it is again regulative in the sense of contributing to maintenance of the normal, though in a wider sense

than before. Thus we have still before us the fact that bodily functions and structures with their immediate environments have the peculiar characteristic of tending very strongly to maintain the normal. The parts and workings of a machine show no such behaviour.

To take another instance: we know from the investigations of Hering and Breuer that distension of the lungs to a certain point inhibits inspiration and initiates expiration, while emptying the lungs to a certain point has the converse effect, these effects being reflexes of which the vagus nerve is an afferent channel. By itself this knowledge was quite unintelligible. It seemed to suggest that inspiration and expiration are events following one another in response to certain stimuli which are quite independent of the gases in the blood, whereas we now know, as already pointed out, that it is the gases in the blood that immediately regulate the breathing. But further investigations have recently shown that the degrees of expansion or contraction of the lungs at which the reflex occurs are dependent on the blood gases. If, for instance, the carbon dioxide in the blood is first reduced by forced breathing, so that the state of apnœa is produced, the slightest expansion of the lungs will initiate expiratory effort, while the slightest contraction will initiate inspiratory effort. Hence the breathing movements are jammed, and if we attempt to apply artificial respiration by Schäfer's or any other method unaccompanied by considerable violence, hardly any air passes in and out. If, on the contrary, excess of CO_2 is allowed to accumulate in the blood, the reflex is so modified as to permit of deep inspirations and expirations. Organic regulation thus

dominates the reflex, and the account of it which has passed muster for fifty years is thus imperfect. A very large and quite common group of clinical symptoms, including those with the military designation of "disordered action of the heart" and "chronic gas poisoning," appears to be due to an upset of this reflex, with consequent very shallow and therefore rapid breathing, and want of oxygen, with all that this brings with it.

When we examine the circulation we find the same kind of constant regulation from minute to minute as in the case of respiration; and it is the breakdown of the regulation that we have to do with in illness. But of this regulation we are often given hardly an inkling in the text-books, though there are abundant and tiresomely minute details about the mechanics of the circulation.

It is the same with the kidneys. There are long and very inconclusive discussions of the possible mechanisms of secretion, but hardly any attention is given to the absolutely dominant fact that, in whatever way the kidneys accomplish it, they are constantly engaged in regulating the composition of the blood with a fineness which is almost incredible till one attempts to measure it quantitatively in the same way as the fineness of regulation of the breathing or circulation is measured.

To whatever part of physiology one turns one finds evidence accumulating of the fineness and omnipresence of organic regulation. One necessarily misses this regulation entirely if one takes processes and organs one by one, and not in relation to the whole life of the organism. Illness is disturbance of organic regulation: consequently physiological teaching which disregards organic

regulation has but little direct reference to medicine, and can be of relatively little help. A capable doctor has to neglect, to a large extent, the physiology he has been taught, and he has to make for himself a new, and often very crude, physiology.

If modern teaching of physiology is defective, so, to a far larger extent, is that of anatomy. Human anatomy frankly professes to deal only with the gross structure exhibited by dead bodies, whereas medicine has to deal with the living body. Now, it makes all the difference whether the body is alive or dead. The living body maintains, by a process of ceaseless and exquisitely regulated activity, the appearance which we call its structure. In disease the regulation is disordered, and in the process of recovery we see the restoration of this regulation. But anatomy disregards completely both the activity and the regulation of it. It frankly does not profess to tell us anything about the conditions which determine the fact that normal and not abnormal structure is present. Of the possible presence of a *vis sculptrix* corresponding to the *vis medicatrix* it has never even heard. "Natural selection or a Creator have just made structure what it is," say the anatomists, "and we cannot give any further information." The medical man has to struggle how he can to solve the problems which arise when either disease or he himself interferes with normal structure. Anatomy does not stretch out even a finger to help him in this struggle: it deals only with the dead. What help there is comes from experimental embryology and physiology, the recent work of the Edinburgh Physiological School being specially prominent in this direction. In this

country the physiologists have annexed to themselves the study of the microscopic structure of the body, besides inventing, in addition, an ultra-microscopic structure. Of the great future science of experimental anatomy only the germs exist at present. Human anatomy behaves as if she had sold her scientific birthright for a sorry mess of "systematic" pottage.

Pathological anatomy has, of course, suffered from the same deficiencies as normal anatomy. To many medical men the pathologist is a sinister figure which stalks behind the chaplain and in front of the undertaker, and which is constantly peering over the shoulder of the consultant and whispering suggestions of morbid changes which, like the normal anatomical structure, just come out of the blue, and which hopelessly sentence a patient to death or permanent disability. My intellectual as well as moral sympathies are all with the cheery general practitioner whose motto is "Never say die," and who flashes defiance at this dismal ghost.

On the side of abnormal function pathology is, of course, quite as active as physiology, but seems to me to suffer grievously from the defects of physiological teaching. For, in the main, experimental pathology sets out with the same limitations that keep the physiologist out of contact with practical medical work. When the normal organic regulation of physiological activity is almost ignored by physiology, the pathologist is, of course, diverted from laying his finger on the nature and causes of failure in the regulation and on the processes which lead to the re-establishment of regulation which constitutes recovery or adaptation.

Let me give one more illustration from my own ex-

perience. Work on the health conditions at metalliferous mines, quarries, and factories brought me into contact with the terrible phthisis mortality which sometimes results from dust inhalation. The effect is mainly due to siliceous dust, such as that from the Craigleith sandstone formerly used in Edinburgh, or from millstone grit, gannister, Transvaal quartzite, or the powdered flint used for pottery work. But in many industries men are also greatly exposed to dust, and even dust consisting largely of crystalline silica; yet no excess of respiratory trouble occurs among them. Coal-miners, for instance, breathe much dust, and with it a great deal of siliceous dust, but suffer even less from phthisis than agricultural labourers; and one finds men who have worked for decades in very dusty crushing mills, where extremely hard stone is crushed, containing 70 per cent. or more of silica, and yet they show no signs of ill effects. It seemed clear that much is hidden behind the name "pneumoconiosis"; but what? Evidently the first thing to do was to find out whether, and by what means, the lungs get rid of a harmless dust, such as coal-dust or shale-dust. The microscopic work was carried out by Mr Mavrogordato at my laboratory, with the financial support of the National Medical Research Committee, and resulted in showing that though with ordinary exposures the harmless dusts enter the lung alveoli in large amounts, the dust is all got rid of after a certain time. It is carried out by dust-collecting cells along several paths. In the case of pure siliceous dust, however, the transport fails, or is very slow, though the dust is collected in cells as before. The dust-containing cells remain, therefore, in the walls of the lung alveoli and

elsewhere, with results which ultimately become disastrous. When, however, there is a mixture of siliceous dust with the ordinary dusts which stimulate transport, the whole of the dust is carried out.

Hence, as soon as we got some understanding of the normal regulation of dust elimination, we could lay our fingers on how this regulation breaks down in the case of pure siliceous dust, and suggest a possible remedy. If we had simply asked what the immediate effects of dust inhalation are, we should have got nowhere; for the immediate effects seem to be much the same for all kinds of dust, and if enough of dust is inhaled rapidly, pathological results follow in all cases. The proverbial black spit of the collier is in reality just as healthy a sign as the increased breathing caused by muscular exertion, or immunity produced by a vaccine.

In connection with the phenomena of immunity, pathology has not waited for physiology, but has gone ahead on the right lines, and practically created a new branch of physiology on the way. In many other directions, however, pathology seems to me to have been kept back by the imperfect conceptions which hamper physiology and anatomy; and this is still more strikingly true of pharmacology. The truth is that anatomy, physiology, pathology, and pharmacology are all branches of the one science of biology, with no definite dividing line between them; and all should be definitely and explicitly based on the distinctively biological conception of organic regulation. This marks them off from other preliminary subjects, such as mathematics, physics, and chemistry.

No doubt I shall be reproached for trying to reintro-

duce obsolete teleological conceptions into physiology and medicine, but I shall not attempt to deal with this reproach now. What I have tried to show is, that whatever may be the ultimate conclusion about teleology, there can be no doubt that practical medicine is based on a teleological conception of the working of the body, and that because physiology, as ordinarily taught at present, ignores this conception, there is but little living contact between physiology and medicine as a curative art. In other words, physiology, and with it the other preparatory biological sciences, is not taking its true place as Institutes of Medicine, to use the Scots name. This is my diagnosis of the main underlying cause of the want of connection between these sciences and medicine.

As to the remedy, this lies mainly in the hands of the teachers; but I think that the defect is now tending to disappear. The days of too exclusive attention to muscle-nerve preparations, the mere physical structure of dead tissues, and the mere chemistry of the body fluids and dead tissues, is past; and human physiology is taking a more and more important place in research and teaching. With the human subject of experiment the teleological mode of approaching physiological problems is inevitable, and *pari passu* physiology is coming closer to medicine. The study of immunity is also tending to bring pathology closer.

I have criticised the present-day teaching of physiology, anatomy, and pathology, but I want now to urge with all the emphasis I can, that whatever may be their present shortcomings, the group of preliminary sciences represented by physiology, anatomy, pathology, and

pharmacology form the future basis of practical medicine. The rest is only subordinate detail, changing from year to year and from place to place, and only surviving through the contributions it is constantly making to these sciences. Practical medicine is one of their active growing points—perhaps I should say their main active growing point—nourished by the mother earth of new experience. The medical art which is not grounded on these sciences is bound to become more and more of an anachronism. Treatment can only be securely founded on a correct and full diagnosis of what is amiss in organic regulation, and how Nature can be aided in restoring the regulation. But diagnosis is far more than the mere giving a name to a morbid condition. The practical problem is always as to how in each particular case there is deviation from health, and how in each particular case Nature can be aided. In solving these problems scientific knowledge is indispensable. It is "with brains, sir," that the physician mixes his prescriptions and the surgeon guides his knife.

This means that the preliminary sciences must go with the medical man to each bedside and guide him at every step. As regards clinical demonstration and instruction in medicine and surgery, I think it means that we must more effectively install the active prosecution of the preliminary sciences at the bedside, and not merely leave scientific investigation behind in special laboratories. The diagnosis and treatment taught to students cannot possibly be progressive unless the teachers are progressive in the personal prosecution of scientific knowledge. At present the majority of medical and surgical teachers are so busily engaged in private practice that they cannot

devote the necessary time to the details of scientific research, with its ever-increasing complexity of methods. I wish, therefore, to make certain suggestions for the remedy of this state of matters.

In the first place, it seems to me essential that real clinical laboratories should be established to help in the investigation of living patients and methods of treatment. A single good room in connection with the service of each visiting member of the hospital staff would probably suffice for this purpose. For the research work to be carried out in each laboratory it would be absolutely necessary to have the services of a competent paid assistant. His duties would be, firstly, to carry on research work under the general direction of the physician or surgeon, and, secondly, to act as the intelligence officer connecting each clinical laboratory with the main university or other laboratories, and with other clinical laboratories. He would have to see to the details of experimental methods, and get information as to how to work them. The apparatus and chemicals would only be what is needed for observations on normal or abnormal human beings, and this apparatus, when done with for the time, could be returned to a storeroom in the hospital, or to any other place from which it had been temporarily borrowed. Experiments requiring the use of animals or of considerable space would be much better done in the main university or other laboratories.

The appointments of such assistants would be very important, and would, I think, be much sought after. The work of these laboratories would bring new life and stimulus into the work of the wards, and would

also, I feel sure, react with equally stimulating effect on the main laboratories. In my own experience, practical human problems have always been an enormous stimulus to new physiological work and new ideas. The study and means of control of chronic diseases would, I think, benefit very particularly from these clinical laboratories.

Another suggestion which I should like to support is that the holders of chairs of systematic medicine or surgery should be freed from private practice. I cannot see how they can efficiently perform their very important duties otherwise, for they ought to keep in close and living contact with all parts of their subject, besides superintending the development of new forms of treatment and scientific investigation in the wards under their charge. The time has come, it seems to me, for placing these chairs on the same footing as other chairs in the Medical Faculty.

In a recent visit to America nothing struck me so much as the extraordinarily rapid development of medical teaching and research in the best universities. In place of the pompous ignorance of physiology and pathology which one meets with so often among medical teachers in Europe, there was everywhere considerable knowledge of, and enthusiastic belief in, scientific methods. Clinical laboratories, and keen young men to work in them, were appearing in all directions. Side by side with this clinical scientific activity there was an equally marked development in the pure scientific laboratories and their research work, and in the broadness of view which goes with originality. Other features were the introduction of whole-time professorships of medicine and surgery,

and the system adopted by some of the leaders in American surgery and medicine of only carrying on private practice in hospitals so organised and staffed that patients could be thoroughly examined, skilfully tended and observed, and placed in the best conditions for successful treatment. I returned home with the strong conviction that we shall soon be left behind in the medical sciences unless we can introduce radical reforms. It was largely this feeling that led me to venture to open the present discussion with the somewhat iconoclastic views and proposals which I have now laid before you.

Let me add some concluding words. A human being is far more than the mere organism with which medicine and surgery are immediately concerned. To a good doctor his patients, as fellow-men, have a value which cannot be measured ; and he has constantly to deal with them on the human side, and adapt his treatment to it. If he fails to do so, he emphatically fails in his duty. In thinking of the scientific side of medical education we are sometimes apt to let the human side slip, and forget that an essential part of medical education consists of those subtle influences, exercised mainly by example, though partly also by special instruction, which teach sympathy with and understanding of human personality. If, therefore, medicine is to have more science and less rule of thumb, let us see to it also that with the science goes more humanity, and, where possible, a broader general education, not in the mere dry bones of the humanities, but on living humanistic lines.

V.

THE THEORY OF DEVELOPMENT BY NATURAL SELECTION.[1]

JUST fifty-eight years ago Charles Darwin published *The Origin of Species*; and it may confidently be said that no book which appeared during the last century has had so great an influence on human thought and human action. The time of its publication coincided not only with great advances in physics and chemistry, but with an enthusiastic attempt among the younger and more progressive physiologists to reach physical and chemical explanations of the phenomena of life—in fact, to convert biology into a department of applied physics and chemistry. The doctrine of natural selection at once became a part of this movement, and has been generally accepted as one of the main supports of the mechanistic theory of life.

The latter theory has been dominant among physiologists for more than half a century, and has been of great service in the development of physiology. But it has now, I think, served its purpose, and is outworn, though still what may be called the orthodox theory among physiologists. What I wish to do to-night is,

[1] A lecture delivered at the Birmingham and Midland Institute, December 10, 1917.

not to criticise Darwin's account of the probable origin of species, but to consider how far this account gives support to the mechanistic theory of life.

Darwin's argument, briefly put, is as follows. Among all classes of organisms there occur variations, however slight, from the average type; and these variations, in accordance with the law of hereditary transmission, tend to be transmitted to offspring. Some of the variations will give the individuals, or their progeny, an advantage in the struggle for existence—a struggle which is constantly going on, and in which, on the whole, but few survive to the reproductive stage out of the germ-cells from each, or each pair, of which the individual develops. As a consequence, the variations which carry with them an advantage in the struggle of the species for existence will tend to survive, and the species will tend to vary as a whole in the corresponding directions. In this way, therefore, a species will, if there is possibility of advantageous alteration, tend to vary as a whole; and under different local conditions of environment the variations will, of course, take different directions, thus producing a variety of species.

Darwin supported his argument by a wealth of concrete observations, taken largely from the experience of breeders of animals and plants under conditions of domestication. It is no wonder that he has convinced the world that species have arisen by development; and I should be the last to doubt this conclusion. But the Darwinian theory has been taken as a support for the mechanistic theory of life. It seemed to his generation to be a tracing of life back towards the mechanical conditions which are at present pictured as existing in

the inorganic world. Another view of the matter is, however, equally possible; and, to me at least, the fact of evolution seems to lead, not towards reduction of the organic to the level of the inorganic, but, on the contrary, towards the raising of the inorganic to the level of the organic. Let us, therefore, examine the nature of Darwin's argument more closely, and in the light of modern physiology.

In the first place, the argument assumes the fact of hereditary transmission, and that variations, in whatever way they arise, are capable of being transmitted. A variation not capable of being transmitted to offspring would be of no account in Darwin's argument. The true significance of the part played by hereditary transmission in the Darwinian theory has, I think, hitherto escaped due recognition.

Let us picture to ourselves what a living adult organism, or even a germ-cell, is on the mechanistic theory. It is a structure, made up of molecules of albumins and numerous other chemical substances, the whole being so arranged that it reacts to the environment in such a way that its characteristic life-history tends to be fulfilled. It differs from simpler inorganic structures in its greater complexity; but if we knew not only the nature and properties of the constituent molecules and the action on them of the physical and chemical environment, but the manner in which they are arranged, we could predict the behaviour of the organism.

Now let us see what conception of hereditary transmission is possible on such a theory. In the process of reproduction an organism, whether it be an adult

organism or only a germ-cell, separates off part of its structure; and this portion grows, and may divide again and again before the first organism is reproduced. Moreover, the process of growth, division, and final reproduction is capable of indefinite repetition, and in ordinary cases two separate organisms—the male and female—combine in the process, and both contribute in the hereditary transmission of character. It thus appears, firstly, that a part, and usually a microscopically minute part, is capable of reproducing the whole: secondly, that each such minute part can reproduce itself indefinitely, and even combine in doing so with other minute parts from another organism.

The mechanistic hypothesis from which we started was that the characteristic properties of the whole organism are due to the arrangement of its separate constituent parts, be they single molecules or aggregates of molecules. But in reproduction the body separates off one of its parts, in which part, of course, the arrangement present in the whole cannot be contained. This part then proceeds to build up the structure again, and may repeat the process indefinitely. If this had been a laboratory experiment specially designed to answer the question whether the behaviour of an organism depends simply on the arrangement of its parts, no more conclusive negative result could have been imagined: for when the arrangement is taken away the behaviour nevertheless returns to what it was.

In the process of reproduction the whole structure, it is true, is not discarded. Certain minute parts are at first preserved intact. But these parts, too, must divide and grow, to provide for future germ-cells. Thus

every part of the structure, every molecule, and every atom, is involved sooner or later in the process of discarding.

In recent times most biologists have been content to leave the main problem of heredity on one side as too difficult for solution at present. But the attempts which have been made to present some sort of solution on mechanistic lines are at least instructive.

There was first the "box-within-box" theory, according to which the complete structure of the adult organism is contained hidden away in the embryo, and within this hidden structure equally complete structures of all future embryos. This grotesque theory need not detain us further, though it is certainly the logical outcome of the mechanistic theory of life.

To come to recent times, an attempt was made by Weismann to simplify the problem by denying the transmission of characters acquired by the organism itself, as distinguished from its germ-cells. Thus simplified, the problem was to see why one germ should be so exactly similar to the germ from which it originated; and this gave rise to Weismann's theory of the continuity of the germ-plasma. He maintained that the germ-material of one generation is directly descended, without intermediate forms, from the germ-material of the preceding generation, and that this helps us to account for germ-cells of the same strain being so similar. He has to admit that the germ-material must have an immensely complex structure, since it determines not only the whole complexity of structure in the adult organism, but also the complexity of the process of development. Nevertheless he proceeds to call the

germ-material "germ-plasma," as if it were a liquid similar to the blood-plasma, and capable of having similar liquid added to or subtracted from it without alteration of its properties.

To speak quite plainly, this theory is completely self-contradictory. A plasma is a liquid containing various kinds of molecules in simple solution, and possibly also aggregates of molecules in suspension. In such a liquid the molecules and aggregates are free to move about, and are in constant and rapid motion. Fixed and definite structure does not exist. For a mechanistic explanation of heredity a most definite structure of inconceivable complexity must be postulated—no mere plasma; and the difficulty of conceiving how this structure reproduces itself remains just as before. Weismann only shifted the difficulty from one place to leave it without the slightest simplification at another. On denying the influence of changes in the somatic cells on the germ-material, the necessity arises of making the structure of the germ-material so much more complex, to account for the fact that both parent and offspring develop similar new characteristics in similar new environments. Whether we regard the germ as very simple or as very complex, the problem remains equally insoluble from a mechanistic standpoint; but if the germ-material is supposed at one and the same time to be an extremely complex and definite structure, and a simple "plasma," the supposition makes sheer nonsense.

Physiologists who have seriously considered the problem of heredity, and yet adhere to the orthodox mechanistic opinions, are, I think, for the most part

now well aware of the difficulty in forming any conception of the mechanism of heredity. They put the matter aside with the excuse that there are many things of which we do not yet understand the mechanism, and that this is one of them. They also argue, though now somewhat faintly, that the success of mechanistic explanations elsewhere in physiology justifies the belief that some day a mechanistic conception of heredity will come into view. This attitude would be justified if it were possible to see any glimmer of a mechanistic explanation of heredity, and if it were actually the case that mechanistic explanations generally showed any signs of fulfilling the hopes that were formed of them about the middle of last century. But the difficulty about heredity is, not that we do not know the details of its mechanism, but that we cannot remotely conceive any possible theory on mechanistic lines, unless it be the inherently ridiculous "box-within-box" theory. Moreover, the difficulty about a mechanistic theory of heredity is only another aspect of difficulties which loom clearer and clearer as physiology advances, and which are inherent in mechanistic theories of all vital processes.

Before going further let me dwell shortly on this last point. What distinguishes living organisms from other things is that they actively maintain their characteristic structure and activities during their life-history. On superficial examination the structure of an organism may appear to be a mere aggregate of material, as does an ordinary inorganic structure. But closer examination shows that living structure is in a constant state of flux—of breaking down and building up of material;

and the more definitely alive any part of an organism appears to be, the more marked is this characteristic. Not only is matter being taken up or given off molecule by molecule; but whole cells or groups of cells are being given off and developed anew. Moreover, we cannot draw any really definite line between an organism and its environment. For instance, the blood and lymph may be regarded either as environment or as parts of the body; and the same is true of the contents of body cavities, such as the gas in the lungs or the food in the alimentary canal, or even of we know not how much of the "contents" of living cells. The environment and the different parts of the body are constantly influencing one another in different ways; but on the whole these activities and influences tend to remain constant or oscillate round a characteristic normal standard. Normal structures, normal environment, and normal activity are clearly bound up together.

When we seek for a mechanistic explanation of the life of an organism the only course is to look for it in the peculiar structure of the body and the nature of the reactions between this structure and the environment. The wonderful delicacy and definiteness in the reactions which are constantly occurring within the body seem to imply a corresponding delicacy and definiteness of structure. But we are soon met by the difficulty that the more delicate the structure must be supposed to be, the more evidently does its existence from moment to moment depend on its immediate environment and on the activities which the influence of the environment is constantly producing in it. We are thus

referred back for explanation from delicacy of structure to constancy of environment. But evidently the constancy in the environment in immediate contact with an organism depends on the organism itself. So we are again referred back to organism, and the upshot of the attempted mechanistic explanation is vain. Structure, environment, and activity are associated in what we recognise as a manner normal to the organism; but of this association we can conceive no possibility of a mechanistic account; and we are no better off if we return to the vitalistic theory still held by a minority of biologists. From the mechanistic standpoint we are thus face to face with a mystery which is just as insoluble in connection with all physiological activity as the mystery of heredity. In both cases we are up against hard facts which cannot be reconciled with any mechanistic conception.

It is impossible to ignore these facts. They come before us at every point in biological investigation. They signify perfectly clearly that in the phenomena of life we have before us a kind of unity which cannot be resolved into simpler elements. This unity of structure, environment, and activity is just life. We cannot resolve life into mechanism, because when we separate a living part from its environment, or suspend its activity, it is at once completely altered. We can take a machine to pieces, or stop its action, without evident alteration to the parts; but we cannot do this with a living organism. Moreover, the unity of a living organism persists: if this were not so, the normals of the organism would not be normals. We must thus recognise that when we say that biology

deals with life we mean that it deals with phenomena which possess the characteristics just mentioned, and which are just those which our ordinary observation and language attribute to life as distinguished from mechanism. For biology the conception of life is fundamental, just as the conception of atoms is fundamental in chemistry.

I have condensed this reasoning into a few words. But for those who wish to follow it in further detail I may perhaps refer to my recently published book on *Organism and Environment*, containing a series of lectures delivered last autumn at Yale University under the Silliman Foundation.

The objection will at once occur that the conception of life just outlined contradicts the fundamental and thoroughly established laws of physics and chemistry. Chemical and physical research show that living organisms, like other material, are made up of atoms and molecules; and exact experiments prove that the law of conservation of energy holds no less rigorously for living organisms than for the rest of the visible universe. Hence the phenomena of life must, in ultimate analysis, be reducible to those of the interaction of atoms and molecules.

The question thus raised is fundamental, and I wish to face it fully and squarely. One way of answering it would be simply to point out that biology, no less than the physical sciences, is concerned with facts. The facts are the primary things; and if physical and chemical facts will not square with those of biology, we cannot for the present help it: biology has at least as good a right to appeal to biological facts as physics and

chemistry have to appeal to facts in their own department of knowledge.

But this attitude leaves us in face of an apparent absolute contradiction, which crops up at every point and paralyses investigation. We must evidently probe deeper, in the faith which is the presupposition of all knowledge, that no real contradiction exists. Let us, then, examine the physical and chemical data with a view to discovering how far we are dealing with established fact, and how far with hypothesis.

I think the discussion of this point will be more intelligible if I give it a concrete form, and I will take as a starting-point the kinetic theory of gases. By starting from the assumption that a gas is an assemblage of immense numbers of free molecules each of which is perfectly elastic, so that it repels anything else on contact, and that each molecule is in very rapid motion, the source of this motion being heat, Waterston, Clausius, and Clerk Maxwell showed that we can predict a number of facts, and in particular those hitherto known only empirically as the so-called gas-laws discovered by Boyle, Charles, and Avogadro, and embodied in the well-known equation $PV = RT$.

When, however, we go back to the actual facts, we find that although for many gases PV is within certain common ranges of pressure and temperature nearly constant at constant temperature, the constancy is only approximate. When P is sufficiently high, or T sufficiently low, the law breaks down in every case, and to different extents and in different directions for different gases. This failure is not merely due to the fact that the molecules themselves have a certain

volume. This could easily be allowed for by modifying the equation. The essential cause is that the molecules attract and combine with one another in various ways which the equation does not express. The ideal gas obeying the equation is a fiction. Thus the equation fails to represent the reality which is there: it only represents a tentative working hypothesis which is good enough for certain immediate practical aims.

We can easily see why the kinetic theory of gases must break down. For there is nothing in the theory to enable us to predict the endless phenomena which appear when molecules come into close proximity with one another under various conditions. Evidently the molecules may, and do, enter into aggregations and "chemical" combinations of all sorts, which can only be discovered empirically. The latent energy which manifests itself in these changes is part of this empirical factor. The molecules may also dissociate into atoms, and, as we now know since the discovery of radio-activity, the atoms may themselves be dissociating, with liberation of vast and hitherto unsuspected stores of energy. The reverse process, with a corresponding locking up of energy, may also be occurring. We are therefore now face to face with a question as to what are the conditions of stability of an atom; and since, as the known facts indicate, atoms are not merely compounds of other atoms similar in kind to those known to us, the conceptions of mass and of energy are themselves under review, and can no longer be regarded as fundamental.

We have become accustomed to the idea that the "laws of Nature" represent truth of universal applica-

tion. But when these laws have to pass, one by one, before the bar of Reason, we see that they have only the limited validity of provisional working hypotheses, although they are indispensable in helping us to bring order and prevision into our perceptions and actions. In other words, they are only ideal fictions. When, therefore, it is argued that the distinctive conception of life is not in accordance with other " laws of Nature " derived solely from past observation of the inorganic world, we are justified in dismissing the argument.

The contention that it must be possible to predict the phenomena of life from the properties of the chemical substances composing the organism must be set aside at once, since the substances we can separate from the living body are evidently altered in behaviour by the separation. From the chemical standpoint a living organism might, perhaps, be regarded as one huge molecule or chemical system of molecules with easily dissociable parts, each containing innumerable unstable side-linkings, constantly taking up and giving off smaller molecules of different sorts from or to the environment. Except from observation of living organisms, we have no knowledge to guide us with regard to the behaviour of such a molecule or the various atomic linkings contained in it. Nor have we any means of predicting, except by actual observation of such a molecule, the liberations or absorptions of free energy associated with the building-up and breaking-down processes in the molecule. All that we ascertain by the measurements which verify the principle of conservation of energy in the living body is that when the organism, or the molecule, has deviated from, and

then returned to, a certain condition, the total energy which has passed in is balanced by that which has passed out. What this means is that *on balance* the organism or molecule has not altered at the end of the period of observation. But the specific peculiarities and liberations of energy in either the individual or the average responses of such an organism or molecule to changes in environment are not such as we can predict from knowledge of its separated component parts, any more than we can predict the behaviour of water, or the energy developed in its formation, from isolated study of the hydrogen and oxygen from which the water originates. The mechanistic argument from the principle of conservation of energy is thus sterile. It is impossible to predict on mechanistic principles the energy transformations in a living organism.

The contention that it must be possible to predict the phenomena of life from isolated study of the material contained in living organisms is on a par with the contention that it must be possible to predict all inorganic phenomena from fundamental mechanical principles. But the operation of such principles can nowhere be found or remotely conceived, except in relation to a fictitious ideal world such as that of the gas equation, or such as that assumed by Laplace when he imagined the world-equation of an omniscient mathematical physicist. Even in the inorganic world actual empirical observation is the evidence before the ultimate court of appeal; and in this court the evidence of biology is just as admissible as any other evidence.

I have tentatively compared a living organism with a huge unstable chemical molecule. In a suitable

environment such a molecule would, like an organism, tend to maintain itself, and would also, like an organism, tend to steady its immediate environment by taking up or splitting off atomic groupings till conditions of equilibrium were established where the processes of taking up and splitting off balanced one another.

So far I think we can get in the endeavour to relate organic to inorganic phenomena. But there is another characteristic feature of living organisms for which we cannot, as yet, point very definitely to any analogy among inorganic phenomena. This is the phenomenon of indefinite growth or assimilation, with associated indefinitely often repeated reproduction of the organism. Equally without analogy is the converse phenomenon of indefinitely repeated local or general discarding of structure or death. I think that probably similar phenomena are present everywhere in the inorganic world; but, if so, we have not as yet seen or interpreted them rightly, and when we do see them our whole outlook on inorganic phenomena will be changed. To put the matter in another way, phenomena of fundamental significance and importance are clearly revealed in the study of living organisms, and have not hitherto been revealed in the study of inorganic phenomena, though perhaps they are beginning to come into view in recent work on the constitution of atoms. In biology we therefore see deeper into the nature of reality than in the physical sciences.

In the ordinary physical or mechanical treatment of Nature we content ourselves with very superficial knowledge such as that represented, for instance, by the gas-law equations or by the law of gravitation,

both of which we know to be only sensibly true when "bodies" are at more than a certain distance from one another. This superficial knowledge is of inestimable practical value in spite of its superficiality. In chemistry we go deeper, and consider what happens when what we interpret as matter is in intimate contact with other matter. In this region we see beyond the superficial generalisations of mechanical physics. In biology we see further still: we make use of the whole of the superficial generalisations presented by physics and chemistry, but we have to interpret them afresh, in view of the new facts which appear in biology, just as we have to re-interpret biological generalisations in view of the new facts revealed in still higher branches of knowledge, such as psychology and ethics.

I know well that this is not the view to which popular natural science has accustomed the world in recent times; but I am convinced that it is the only view which can be reconciled with the facts and with the implicit claims of every kind of real scientific investigation. Popular natural science has suffered severely from what, in vulgar language, is called "swollen head"; and the sooner this is generally recognised the better. When we refer back to actual observation the abstractions of popular natural science appear in their proper light.

I have tried to show that there neither is nor can be any mechanistic explanation of heredity and nutritive activity, which are integral parts of Darwin's theory. I now wish to examine more closely the fact of variation, which is another integral part. A variation in the biological sense is something that has relative permanence

and stability, such as the normal characteristics of an organism have. These characteristics, whether of structure, or activity, or immediate environment, hang together as a whole. We cannot alter them piece by piece, simply because they hang together as a whole. But an organism is bound up with its environment; and though it clearly tends to keep its environment normal, and particularly its immediate environment—for instance the blood, or the air in the lungs, or the immediately available food supply in the alimentary canal—this is never a perfect process. With any gross or continuously acting change in external environment the whole organism must vary to some extent.

When we examine physiologically the variations which occur in response to changes in environment we find that they are "adaptive" changes. That is to say, they are changes of a compensatory character, or of such a nature that the general disturbances associated with the altered environment are reduced to a minimum. The existence of a tendency to compensatory adaptation to all the accidents and ills of life is the great central fact on which medicine and surgery are based. Their function is to assist in this adaptation. Without its existence they would be powerless. If wounds did not tend to heal, and the body generally to adapt itself to any remaining abnormality; if damaged tissues did not tend to repel the attacks of disease, and establish a new normal, no medical or surgical skill would be of the slightest use. And, similarly, if the body were not constantly adapting itself to the indefinitely varying changes in environment which are constantly occurring, life would be non-existent. Life is in reality just continuous

adaptation—a continuous struggle for the realisation of organic order.

These adaptive changes are no mere "functional" adaptations: they are also structural, and modern physiology shows clearly that the distinction between structural and functional change in a living organism is illusory, and never stands examination. To explain the adaptive changes which are constantly occurring everywhere in living organisms—for instance, reproduction of lost or injured parts, or those marvellous functional adaptations which modern surgery has learnt to take such striking advantage of, the mechanistic theory is forced to assume the existence of absolutely endless subsidiary reproductive and compensatory mechanisms in the body. Such assumptions are just as grotesque as the old "box-within-box" theory of reproduction.

If the disturbing factor in the environment is passing, and of ordinary occurrence, the adaptive change simply restores the previous normal. But when the disturbing factor is unusual, or lasting, something more than a return to the previous normal occurs: for we then observe what is ordinarily recognised as adaptation. Common examples of this are the physiological adaptations which occur in learning some new operation, in training for hard physical exertion, in resisting infection or poisons, in becoming acclimatised to the shortage of oxygen at high altitudes, or in learning to digest new kinds of food. The new organic experiences involved leave their mark behind in the form of definite adaptations, involving not merely functional, but also structural change in the organism.

What distinguishes adaptations from other changes

is that in the adaptation the identity of the organism is preserved. We can always trace in the unadapted organism the rudiments of what has become more evident in the adapted organism. In this case there is development, and not mere change in the physical sense. Alongside of what is ordinarily called development, there may occur the converse process of degeneration, where some structure or capacity which was well developed before has become more rudimentary; and this, of course, is a common occurrence. In man, for instance, the organs and capacities connected with smell have become comparatively rudimentary; and in the individual man excessive specialisation in one direction is apt to be at the expense of atrophy of other capacities. But the maintenance of physiological and structural identity is no less evident in degeneration than in development.

Variation of all kinds in the individual organism seems to be of the nature of development or degeneration. This implies that in all variation the specific nature of the organism expresses itself. The new environment to which the variation is a response has definitely become, as it were, a part of the organism's normal environment, and so an element in the unity which, as already explained, constitutes its life.

According to the hypothesis put forward by Weismann, and adopted by many biologists, acquired characters are not transferred from the parent organism to the germ-cells, and are consequently not inherited. I have already pointed out that this hypothesis does not simplify in any way the problem of heredity. There is also direct experimental evidence against it, which, however, I can hardly discuss at present. What I do

wish to emphasise, however, is the great improbability, on general grounds, of the hypothesis. The further physiological knowledge advances, the more evident does it become that each part and each activity of the body is intimately dependent on the other parts and activities. Life is a whole of which the elements cannot be isolated without changing them. The whole is in all the parts, including the environment. Now, Weismann's hypothesis assumes that the germ-cells are no more a part of this whole than if they were mere parasites. There is no warrant for such an assumption, and every known relevant fact seems to me against it. Just as the presence of the germ-cells, and their development, influences the parent organism profoundly, so, I think we must assume, do changes in the parent organism influence the germ-cells. They are part of that whole which is in all the parts and their environments; and, if so, acquired characters must be capable of hereditary transmission.

It takes time, and often frequent repetition, to develop adaptation. Otherwise the lesson is, as it were, forgotten, and but little progress results. An adaptation which may not remain fixed in even the tissues of the parent organism can hardly be expected to be easily transmitted to offspring; but that there nevertheless is transmission of adaptations which generation after generation of parent organisms undergo, I can feel no doubt. The adaptive response will thus become more and more easy till at last it becomes established as a normal event in individual development—in other words, a definite race-adaptation.

Weismann's theory of the physiological isolation of

the germ-cells carries with it the corollary that all true or heritable variation is primary variation of the germ-cell. But as different individuals of a species vary in spite of this supposed physiological isolation, how does the variation occur? To help in this dilemma, the large and very important class of facts associated with the name of the Abbé Mendel has been invoked. He made the original definite discovery that in sexual reproduction the characters inherited are not an evenly-blended mixture of those of the parents, but that some, at least, are exclusively derived from one parent, or may even be missing; and that the proportion in which these "Mendelian" characters, or "factors," are distributed among the progeny can often be calculated on the abstract theory of probabilities—that is to say, as a mere matter of chance. "Factors" may also influence one another in different ways, and may thus be either more or less capable of combination in one individual. In these ways there is great scope for variation in progeny, apart altogether from immediate influence on the developed organism of varying environment. On the theory that the germ-cells are physiologically isolated from the parent organism and its environment, we can thus account for variation, provided we assume that variation is due to a mere re-shuffling, or dropping out, of original "factors"; and this is the substance of the position taken up by Professor Bateson in his Presidential Address at the meeting of the British Association in 1914. This position, as is recognised by Bateson, tends, logically, towards the view that all the "factors" were present in the original amœbæ, or whatever other lower organisms we are all descended from. On the mechan-

istic theory, it would thus be necessary to assume that within the bodies of these primitive organisms there is somewhere hidden away all the inconceivable complexity of structure required to account for all future development. It is only a step further to represent this complexity of structure as present in the carbon, nitrogen, and other atoms out of which the primeval organisms arose. In presence of such hypotheses, one feels that it is high time to return to sanity. Nevertheless, they seem to be the logical outcome of a mechanistic interpretation of inheritance.

When we start from the fundamental biological conception that life is a whole which determines the nature and activity of its parts, and that is constantly maintaining itself actively by a process of nutrition, we at once get rid of this terrible burden of inconceivable mechanism. The complexity is then no longer in the structure of the parts, but in their relation to the whole. The germ material is no longer complex mechanically, but only complex in its physiological relations to environment; and whatever an atom may be, its peculiar behaviour in the living body is wrapped up in the uniqueness of its relations there. The germ reproduces the whole organism just as every individual cell or part of a cell in the body is constantly renewing itself in nutrition. There is every gradation between complete reproduction and ordinary nutritive changes such as we can follow by chemical methods, or with the microscope, in gland-cells, or with the naked eye in the reproduction of lost parts, or in the shedding and replacement of leaves on a tree. In the process of reproduction, just as in the process of nutrition, the organism builds the missing structure up

again from the stage at which this structure is in defect, repeating in outline the slow stages of ancestral history. Progress is easy and rapid, because the proper environment and proper stimuli are provided in advance; just as a man who is given proper tools and material, and knows what is required, rapidly succeeds in doing work for which it took centuries to establish the necessary conditions.

But if not mechanism, what is it in a living thing, or in the atoms composing it, that makes it react in this particular way to environment? Saturated as we are with mechanistic conceptions of reality, this question inevitably arises. The action seems to depend somehow on the properties of the atoms. An atom for ordinary chemistry is a material unit of a certain mass, and which is found to possess one, two, or more definite "affinities" for other atoms. But when we follow the atom into the living body we find that its properties cannot be thus summed up simply: for the specific peculiarities connected with different saturations of the affinities are endless; and evidently we have also to do with accessory affinities manifesting themselves in the formation of hydrates, crystals, liquids, solutions, and various other complexes. In all this complexity of properties we lose sight of the old simple atom. The conception of it as a "thing" with definable properties has failed us. To define the "thing" which we call an atom, and which at first seemed so simple, we should have to define the whole universe of "things." The conception of a "thing," or material unit, is thus useless in the interpretation of distinctively biological facts.

To the question why living organisms behave as they

do, the only answer is that it is part of the nature of reality that they do so. It is only from actual observation of them that we can predict their behaviour; and to predict we must make use, not of the conception of "things," and their definite and limited "properties," but of the distinctive conception, based on actual observation, of life. The ideal conceptions of the physical sciences are good enough tools for many practical purposes, but not for grappling with the phenomena of life.

Darwin emphasised the fact of variation, but without pointing out its characteristic feature as adaptation. To my mind this is a serious defect in his argument. Organisms struggle, not for any sort of existence, but for their own specific sort of existence; and in whatever direction heritable variation may occur, and whether it be in the direction of further development or of degeneration, the variation has the distinctive character of adaptation. In Mendelian variations, no less than in other variations, organic wholeness and continuity express themselves clearly. In the structural and functional abnormalities or variations resulting from the accidents of the reproductive process, this wholeness and continuity are just as evident as in the case of injuries or diseases which have been recovered from.

From the point of view of pure biology, the struggle for existence is a blind struggle. But in so far as organisms are conscious this is no longer the case, and the Darwinian theory does not apply. Adaptation is no longer blind. I do not, however, propose to discuss in this lecture the significance for evolution of psychical facts.

The prevailing popular physiology of Darwin's time

was essentially mechanistic. To realise this one has only to glance at books of the type of Paley's *Evidences of Christianity*, with its comparison of the living body to the machinery of a watch. Had Darwin made an actual physiological study of variation in the individual in response to changes or accidents of environment, I think that with his singularly acute outlook he would soon have seen that the mechanistic theory of life cannot be reconciled with the fact of evolution. If the mechanistic theory were correct, Darwin's own expression, "the struggle for existence," would cease to have any meaning: for matter on the mechanistic hypothesis cannot help existing, and cannot "exist" any better in one form than in another. But the very life of an organism is, as I have tried to show, a constant struggle for definite order—a constant adapting. In the evolution of living organisms we thus see a progressive evolution of order out of chaos. The imperfection of the order, as Darwin showed, is bound up with the development. But for either struggle or development to occur living organisms must have the distinctive characters of living organisms; and development is the outcome of life, not of mechanism. The further back, therefore, we can trace the course of development, the further we are pushing biological interpretations towards that region of our relative ignorance which we call the inorganic world; and this is the special point which I set out to make.

Perhaps I may be asked whether it matters to us what particular view we take of life, evolution, and the inorganic world. To me it seems to matter a great deal. Some members of my audience have probably read a

remarkable book, published this year by Professor Pringle Pattison, of Edinburgh, and containing his Gifford Lectures on *The Idea of God.* The fourth chapter is entitled "The Liberating Influence of Biology"; and in it he points out the great importance of biological advance on the lines which I have been indicating, in delivering the world from what he rightly calls "the bad dream of naturalism."

Pringle Pattison's book is a singularly able and clearly written statement of the philosophical position generally known, for want of a better term, as idealism; and perhaps I need hardly say that it is idealism in its applications to natural science that I have been preaching to you to-night. Idealism in its modern form traces its descent from Locke, Berkeley, and Hume. The growth of the physical sciences in the preceding centuries had led, and was steadily leading further, towards the view that whatever somewhat shadowy reality there may be apart from the material reality with which physical science deals, there is at any rate no doubt about this material reality. Bishop Berkeley and David Hume pointed out, however, that if we start from the assumption of this physical reality, including that of our own bodies, we are led to the conclusion that all we can know is made up of the "impressions" which the material world makes upon us. We can have no direct knowledge of the material world. We cannot even know that it really exists; and the world which seems to our senses so clear and solid has therefore only a subjective existence. Sensations or "impressions" are thus the ultimate stuff out of which the whole world of our experience is made. This was a complete turning

of the tables on the claims of physical science; but no one has ever found any way of escape from Hume's *reductio ad absurdum* of these claims.

The next great step taken was by Immanuel Kant. He showed that when "sensations" or "impressions" are examined they are always found to carry with them relations to the unity of the percipient mind, as well as to relations of time, space, and causal connection, just as in what we ordinarily call the "real" world. He therefore concluded that though we cannot know the "things in themselves" that are behind the "impressions," order and connection are imposed on them by the percipient mind, and the physical world appears to us as it does, just because the forms in which this order is imposed are what they are. Kant enumerated the general forms, or categories, under which the mind orders its impressions. He included time and space relations, and those of substance and of cause and effect, but excluded final causes, including the distinctive conception of life. In the realm of what Kant calls the "Understanding" as distinct from Reason, and what other writers, including, in recent times, Bergson, call the Intellect, there is no place for such conceptions. In this way Kant made his peace with the claims of non-biological natural science, so that Kantians, though still idealists, have been among the strongest supporters of a mechanistic view of life. We must look on life as mechanism, they say, just because our minds are so constituted that we cannot do otherwise.

Kant's most famous successor, Hegel, rejected the "thing in itself" as an unreal shadow, and thus became what is known as an "absolute idealist." For absolute

idealism all that exists is within mind, though not mere individual mind, but Absolute Mind. Hegel also showed that Kant's general forms or categories are far too limited, and that the general conceptions which we apply to life and human activity must also be included among the categories. Finally he pointed out—and this was his greatest contribution—that the categories are organically related to one another, the lower being nothing but imperfect forms of the higher, which are, as it were, the truth or fully expressed implication of the lower.

To Hegel Nature appeared as a realm of what one may call fossilised categories; and he sought to describe Nature on this theory in his Philosophy of Nature. But this amounted to shackling the investigation of Nature, just as Kant had shackled it in still narrower bonds of mechanistic interpretation. The later idealism which has developed in Great Britain has cast off these shackles, including the Kantian and Bergsonian mechanistic shackles, and of course also the time-honoured claim of popular natural science that matter as such is something which has absolute reality.

Idealism has thus brought philosophy into real and living touch with living experimental science and living concrete experience. In the interpretation of Nature and of the whole of our experience thought and investigation are left free to use what provisional interpretations are found helpful, provided the provisional character of these interpretations is recognised—provided, that is to say, that theory does not outstrip verification. Science gives the high-power; but only partial views which furnish detail: philosophy gives the low-power and general view that enables us to correct, and helps

us to interpret, the high-power views by seeing experience whole. In the high-power views the outlines are detailed, but imperfect. How very imperfect, for instance, our interpretations of the physical world are I have tried to illustrate to you to-night. In biology we get a lower-power view, by which, though we lose in detail, we can correct misinterpretations of the high-power view of physics and chemistry. In what are called the humanistic branches of knowledge we can go further still in this correction, provided they deal, as they ought to deal, not with trivial detail, but with the development and practical application of great ideas, including scientific ideas. In philosophy or religion—for religion, whether in a crude or in a highly developed form, cannot be distinguished from philosophy — we attempt to survey and give a general interpretation of the whole of our experience.

To many it has seemed that natural science along with its practical application has destroyed the old spiritual view of things—has shown it to be mere illusion and superstition. The idealistic philosophy bids us to look deeper—to look at facts and not merely at theories, and to look at them as a whole.

As I write my lecture there occurs to me something which I witnessed nearly ten years ago near this lecture hall. A large coal mine on the outskirts of Birmingham was on fire. The fire had occurred just at the bottom of the downcast shaft, about 2000 feet below the surface; and smoke and poisonous gas were being carried by the air-current all over the mine, in which a number of miners were cut off. We knew, however, that there were men underground who, if they had not fallen

(as unfortunately they had), would understand how to short-circuit the smoke and gather the other men into a place of safety till the fire could be dealt with. It was found quite impossible, however, to get to the fire, the roaring and crackling of which could be heard at the top of the shaft. A band of Yorkshiremen had meanwhile hurried to the mine with rescue apparatus for penetrating poisonous air. Again and again they, as well as the manager, went down the other shaft through the smoke, and two of them got half a mile into the workings in the hope of finding and helping any men who were alive. But one of the two, John Welsby, was overcome by heat on the way back after a fruitless quest, and his oxygen cylinder became exhausted. His companion just managed to reach the shaft and stagger into the cage. A determined attempt was at once made by two of his comrades to reach Welsby, but failed, as the smoke on the road was now so thick that they could hardly even see the light of their electric lamps a foot away. The air in the fan-drift had also become so poisonous that there was soon no hope of Welsby being still alive. I well remember the general despair, and the helpless, aimless crowd of men round the pit-head.

We went back to the colliery office to consider what more could be done, and after an anxious consultation it was decided to reverse the ventilation as soon as possible, so as to carry the poisonous smoke straight up the ordinary downcast shaft and draw fresh air down the other shaft and through the workings. It was about one in the morning, and immediately the decision was come to the under-manager went out to arrange

for the necessary work of digging a covered trench so as to connect the downcast shaft with the fan, and thus enable it to draw air from the downcast instead of the upcast shaft. I followed to the pit-head three or four minutes later, and was amazed to find that the helpless crowd was gone. Picks and shovels had appeared as if by magic, and the whole of the men were hard at work along the line of the trench. In case the fan did not prove powerful enough to turn the air, a message was also sent through to a Yorkshire pit where there was a small but very powerful fan in use for experiments; and within a few hours the Yorkshiremen had got the fan on the rails, and the railwaymen had hurried it through to Birmingham.

These were the facts; but what light can natural science throw on them? It can tell us that the actions of all those concerned were bound up with endless physiological processes occurring in their bodies. Auditory or visual stimuli of different kinds started the train of complicated movements which brought us together at the pit-head and guided all the movements of those concerned. It was again an auditory stimulus that suddenly brought order and activity into the aimless crowd. It was a constant supply of oxygen and oxidisable food-material properly directed by the action of lungs, heart, liver, nervous system, and various other organs, that made the movements possible. Had any one of these factors been absent the result would have been different. If, for instance, their supra-renal glands had failed to respond, the brave Yorkshiremen would probably have shrunk back in terror before the smoke, heat, and poisonous air. At no one point can natural

science discover a soul which directed all the bodily movements and processes ; and in any case no psychological theory based on self-interest would explain the actual course taken by the men : for they clearly acted with very little regard to either their individual bodies or their individual souls. They acted just as their comrades at the front are now acting, in the midst of mud and water, bursting shells, flying bullets, and poisonous gas. To the high-power view of natural science we seem lost in a maze of physiological processes ; but we are pulled up at once if we attempt to belittle the importance of any one of these processes, for each one of them can be shown to be essential.

Now idealism points out that what natural science has told us does not express the reality itself, any more than the ideal molecules of the kinetic theory of gases represent the real molecules. Outlined by the ideal shadows which natural science shows us one by one, there is a world of reality which reveals itself when we look at them as a whole. It is only through the shadows that the reality appears ; the more of them we can see the fuller become the outlines of the reality. Idealism does not look away from the shadows to some world of mystery : it points to the reality traced by the shadows themselves when they are looked at as a whole, just as a picture is seen when we look at the strokes of paint as a whole, or music is heard when we take in the notes as a whole.

The reality to which idealism ultimately points us is a reality of order and unity, in which every detail has the dignity and value which its participation in this reality confers. In other words, the only real world

for idealism is the spiritual world—that world which our great religious teachers, great poets, and great artists, have constantly sought to reveal.

I have tried to indicate in this lecture the connection between the work of Charles Darwin and modern idealism, and to show you why *The Origin of Species*, so far from giving any support to the mechanistic view of reality, takes us straight in an opposite direction. Who was " on the side of the angels " in the historic discussion at the Oxford meeting of the British Association? Was it Charles Darwin, or was it the well-meaning bishops and others who opposed his views? I think it was Charles Darwin.

VI.

ARE PHYSICAL, BIOLOGICAL, AND PSYCHOLOGICAL CATEGORIES IRREDUCIBLE ? [1]

THE subject of this discussion, as I understand it, is whether the general conceptions or "categories" ordinarily used in interpreting physical, biological, and psychological phenomena are essentially different and irreconcilable with one another.

In approaching this question I think we must carefully distinguish between the conceptions, or, as I should prefer to say, working hypotheses, which we commonly use in interpreting reality, and that reality itself. The discussion applies to our working hypotheses or categories; and I propose to maintain that our ordinary working conceptions of what we regard as physical, biological, and psychological phenomena are not only different, but irreducible to one another.

I will deal first with the difference between physical and biological interpretations of experience. The theory which aims at interpreting the phenomena of life as nothing but physical and chemical phenomena, accompanied, it may be, by consciousness, is generally known as the mechanistic theory of life. The theory which,

[1] Opening paper of a symposium, Aristotelian Society, July 6, 1918.

on the contrary, interprets biological phenomena in terms of a special conception based on the observation of life itself may be called the biological theory.

Of these opposing theories each seeks to interpret the same facts in its own way, and the one way is completely different from the other. But there is also an intermediate theory — that known as vitalism. The vitalists accept as true, so far as it goes, the physical and chemical interpretation of the phenomena connected with living organisms, but maintain that in living organisms we must, in addition, assume the existence of something quite distinct which interferes with and guides the physical and chemical reactions. This something has been called "vital force," "the vital principle," or, to use Driesch's expression, "entelechy." So long as the vitalists confine themselves to merely pointing out the deficiencies of the purely mechanistic theory, the evidence which they bring forward is so strong that it seems to me to be unanswerable. When, however, they try to define vitalism on its positive side, the result is quite indefinite. The something which was supposed to interfere from without in the physical and chemical reactions can always be shown by experiment to be dependent on what were admitted to be physical and chemical conditions, though there is no explanation of how these conditions bring about the actual results. Vitalism thus represents no clearly definable working hypothesis, and for this reason I do not propose to consider it further. Similar objections apply to the corresponding animistic theory in psychology.

I shall now try to present shortly the mechanistic argument, and what seem to me its fatally weak points.

The conception of a living organism as a mechanism is in some respects quite natural and very useful. We can, for instance, understand up to a certain point the movements of the limbs if we regard the bones as levers acted on by the contractions of the muscles. It is equally natural to seek for corresponding mechanical explanation of the contraction of muscle; and though definite progress in this direction has hitherto been limited, I feel confident that we are on the eve of such progress. When we turn to any other form of bodily activity we find similarly that physical and chemical explanations will carry us a long step forwards. Thus the chemistry of the blood enables us to see exactly how oxygen is carried from the lungs to the tissues, and carbon dioxide is carried from the tissues to the lungs: the chemistry of the digestive secretions enables us to understand the chemical changes in digestion; and the structure of the eye and the laws of optics show us how an image is formed on the retina. At first sight, therefore, it seems justifiable to assume that if our knowledge of the chemistry and physics of the living body were sufficiently complete, we could explain completely all the phenomena occurring in living organisms.

It used often to be stated confidently that the development of physiology shows a continuous advance towards a mechanical explanation of life; and this statement is at present widely accepted. It is certainly true that physical and chemical explanations are being profitably applied to more and more of the phenomena associated with life. It is, however, equally true that more and more of these phenomena are being found to be quite insusceptible of the simple mechanical explanations

which were formerly given of them. Fifty years ago many physiological processes which, from a physical and chemical standpoint, are now seen to be extremely complex and obscure, were regarded as quite simple. I need only refer to such activities as the oxidative processes in living tissues, the processes of secretion and absorption, or reflex action. There is a prevalent idea that the progress of chemistry, and particularly of physical chemistry, has furnished explanations of these processes. This is most certainly not the case. What physical chemistry has helped us to do is to obtain measures of the processes in the living body; but the results of the measurements have been to show with ever-increasing clearness that the processes in the living body do not correspond with our conceptions of those in non-living structures, and that we are not remotely in sight of mechanical explanations of the former.

As an example I need only take the case of the exquisitely thin and delicate living membrane which separates the blood in the lung capillaries from the air in the alveoli or air-cells of the lungs. A short time ago it was assumed that this membrane plays only the passive part which we regard a non-living membrane as playing, and allows oxygen to diffuse through just as a non-living membrane would. On applying accurate methods of measurement, we found that whenever there is need for an extra supply of oxygen, as, for instance, during muscular exertion, the membrane assumes an active *rôle*, and pushes oxygen inwards, without regard to the mechanical laws of diffusion. In this respect the alveolar epithelium acts just like epithelium of the swim-bladder, or that of the kidney or any other gland, or the

alimentary canal. The progress of physical chemistry is enabling us to distinguish sharply between physiological activity and the processes occurring in non-living structures; and the establishment of the distinction is sweeping away the easy-going mechanistic explanations which became current during the latter half of last century.

On the whole there is no evidence of real progress towards a mechanistic explanation of life; and those physiologists who still believe that the mechanistic line of attack is the right one are compelled to justify their belief on general philosophical grounds. We ought, they say, to advance from the simple to the complex; from the sure and familiar ground of physics and chemistry to the unknown ground of biology. Practically speaking, they argue that life *must* be a mechanical process, although at present we cannot understand the mechanism.

Now I wish to go straight to the point, and explain why, as it seems to me, life cannot be regarded as a mechanical process. A living organism differs in this respect from any mechanism which we can construct or conceive, that it forms itself and keeps itself in working order and activity. Bearing this in mind, let us look again at the various apparent mechanisms previously referred to. The bones and muscles involved in limb-movements have not only developed into the particular arrangement which renders them efficient, but from hour to hour and day to day nutritive activities are occurring in them which keep this arrangement intact. Moreover, the actual movements are, apart altogether from conscious interference, guided and controlled at every

point. These are facts which the mechanical explanation does not account for.

When we look closely into the changes occurring in a muscle doing muscular work we see that reproduction of the muscular substance is an integral part of these changes. The wonderfully beautiful balance of chemical composition which enables the blood to perform correctly its work in carrying oxygen and carbon dioxide depends no less evidently on constant and minute regulation. The formation and liberation of the digestive ferments is likewise minutely regulated ; and the same is true of the exact form and optical properties of the refractive structures of the eye. Moreover, the whole of these wonderfully delicately-controlled mechanisms have originally developed from a single cell containing no trace of the future structures.

It is thus evident that, although we find within the living body many phenomena which, so long as we do not look closely, can be interpreted satisfactorily as physical and chemical mechanism, there are side by side other phenomena for which the possibility of such interpretation seems to be absent. The mechanists assume that the bodily mechanisms are so constructed as to maintain, repair, and reproduce themselves. In the long process of natural selection, mechanisms of this sort have, they suggest, been evolved gradually.

Let us examine this hypothesis. When we state an event in mechanical terms we state it as a necessary result of certain simple properties of separate parts which interact in the event. Thus it is through the interaction of rigid bones of a certain configuration with contractile muscles attached to them at certain points

that we explain the movements of a limb. Similarly, it is in terms of the interaction of oxygen molecules with the molecules of hæmoglobin and other substances in blood that we explain the taking up of oxygen by venous blood. The essence of the explanation or re-statement of the event is that, after due investigation, we have assumed that the parts interacting in the event have certain simple and definite properties, so that they always react in the same way under the same conditions. For a mechanical explanation the reacting parts must first be given. Unless an arrangement of parts with definite properties is given it is meaningless to speak of mechanical explanation.

To postulate the existence of a self-producing or self-maintaining mechanism is thus to postulate something to which no meaning can be attached. Meaningless terms are sometimes used by physiologists; but there is none so absolutely meaningless as the expression "mechanism of reproduction." Any mechanism there may be in the parent organism is absent in the process of reproduction, and must reconstitute itself at each generation, since the parent organism is reproduced from a mere tiny speck of its own body. There can be no "mechanism" of reproduction. The idea of a mechanism which is constantly maintaining or reproducing its own structure is self-contradictory. A mechanism which reproduced itself would be a mechanism without parts, and therefore not a mechanism.

Let us try to get nearer to what the self-reproduction and self-maintenance of an organism implies. Perhaps the clearest analogy in the inorganic world to the reproduction of an organism is the reproduction of a

crystal. By increasing the external pressure or adding heat, we can cause a crystal of ice to waste away by melting. If, however, we remove the pressure or the heat, the crystal reforms and grows to its former size. We can also, with proper precautions, cool water to below the freezing-point without any ice forming. But if to the supercooled water we add the smallest crystal of ice, it rapidly grows into a larger crystal, just as the germ of an organism grows. The molecules of water possess the property of attracting one another in such a way as to produce mutual orientation or arrangement, in which they take up more space than when they were present as a mere mobile crowd in the liquid state ; and in the starting of the process of orientation some initial hindrance has to be overcome, so that crystallisation occurs far more readily if it is given a start. We must assume that each molecule possesses the property of so attracting each other molecule as to produce the mutual orientation if there is no hindrance from pressure or from the molecular agitation due to heat, or from other causes.

An organism maintains itself through a balance between constant loss and gain, whereas the crystal of water seems at first sight not to change except by growth or melting away. When we look closer, however, we find that the crystal has a vapour pressure. It is therefore constantly giving off, and must be equally constantly taking up, water-molecules from its environment. Hence in this respect also it resembles an organism.

Where the resemblance fails is that the arrangement of the molecules in the crystal is mere repetition, whereas

in the organism there is individual variety of detail, and yet perfectly definite and specific unity of plan. For the formation of the crystal it is necessary that each molecule of water should have the property of tending to orientate itself to any other in a certain definite manner. Mere central forces of attraction do not explain the formation of a crystal from molecules or of a molecule from atoms. Similarly, in the development of an organism we seem bound to assume that the germ has the property of tending to orientate towards itself certain surrounding molecules in the specific arrangement of the fully developed organism, and that these surrounding molecules have corresponding properties.

It may be pointed out that this is no explanation. Nor is it meant to be an explanation. It is a mere general statement of what appear to be the facts of observation. In mechanical physics we have become accustomed to think of molecules or atoms as quite simple things with easily definable properties, such as mass, extension, and central forces of attraction. For biology, the properties which must be assumed in the unit of living structure are enormously more complex, and are only capable at present of statement in general terms. It is solely from previous actual observation that we can predict how the living structure will behave, and we can only do so if the environment is about the same as in the previous observation.

Practically, therefore, we must look upon organism and environment as one interconnected whole which, as a matter of empirical fact, tends to maintain itself, just as a crystal and its mother-liquor do, or a molecule and the solution in which it has formed. From no

elementary mechanical principles can we deduce the behaviour of even the molecule of water in crystallisation; and similarly, from no elementary physical or chemical principles can we deduce the behaviour of the organism. It is owing to this empirical fact that the ordinary working hypotheses of physics and chemistry are irreconcilable with those of biology.

The tacit assumption is often made that in mechanical physics we reach a definition of the ultimate reality of which the visible world consists. For many practical purposes this definition, it is true, suffices. But even in connection with heat, light, and electricity, the definition is insufficient. In chemistry it breaks down still more, and in biology the breakdown is complete. Like pure mathematics, mechanical physics is only an abstract science. We can use it for certain practical purposes, but it tells us only a very little about reality, and in only a very imperfect form.

Let me illustrate my meaning by reference to the kinetic theory of gases—a subject which has been specially engaging me lately. For the kinetic theory of gases, a gas is an assembly of molecules kept in motion by heat, with the necessary consequence that each molecule, whatever its mass may be, possesses on an average the same amount of kinetic energy. Hence an equal number of gas molecules will always produce the same bombardment pressure at the same temperature, and from this pressure we obtain an absolute scale of temperature. In this way we can predict from the theory the three well-known "gas-laws," called, after their discoverers, Boyle's, Charles's and Avogadro's laws. These laws are embodied in the equation $PV = RT$, where P = pressure,

V = volume occupied by one gramme-molecule of gas, T = absolute temperature, and R is a constant for any gas.

Now, it is evident that this equation can only hold good if molecules are regarded as points with mass, but without extension. Some mathematical physicists have clung tenaciously to this idea and to the equation. There we must leave them, because we are not dealing with mathematical figments, but with reality in so far as it is revealed to us in experience. As a matter of fact, the equation $PV = RT$ has only the appearance of holding within certain limits of temperature and pressure. If the temperature falls or the pressure increases sufficiently, the value of PV becomes greater than RT, because the volume of the molecules themselves begins to count. Hence, if we call v the volume occupied by the molecules, we must alter the equation to $P(V-v) = RT$.

If the molecules were simply indifferent to one another, so that they merely repelled one another on contact, we should now have an equation expressing the behaviour of a gaseous substance. But, as a matter of fact, even the amended equation does not express the behaviour of actual gases, for, with sufficient cooling, gases condense to liquids. The molecules attract one another, and with cooling their kinetic energy is reduced progressively so that on an average a constantly increasing proportion of them must be within their mutual spheres of attraction, like the bodies in a solar system, and hence exercise no external pressure. We must, therefore, alter the significance of P, so that it means, not external, but intermolecular pressure. We can, then, as I have elsewhere endeavoured to show, not only extend

the gas-laws to liquids, but by means of them predict with great accuracy a very large number of facts.

There remain other facts, however, which we cannot predict, for with sufficient further fall of temperature a liquefied gas crystallises. It doing so it may, like water or molten iron, increase in bulk. Now, the simple assumptions on which the kinetic theory of gases and liquids is based are insufficient to explain the phenomena of crystallisation, with the accompanying abrupt change of volume and of other properties. We must, therefore, assume, not merely that the molecules attract one another in the directions joining their centres, after the manner of gravitation, but that they tend to assume a definite position, pole to pole, in relation to one another, and actually assume this position as soon as their mutual movements, due to heat, are insufficient to prevent them from doing so. The liquid thus crystallises at a perfectly definite temperature, unless its enormous intermolecular pressure is sensibly increased by added external pressure.

This shows us that when we look closely at actual molecules we are forced to the conclusion that the tendency to take specific form or arrangement is always present in molecules, and therefore in what we call matter. We cannot sum up the properties of molecules in the conceptions of mass, extension, and central forces proportional to mass, in accordance with the fundamental physical conceptions of Newton. The actual properties of molecules can only be expressed in terms of their potential orientations to various other kinds of molecules; and when we pass beyond the comparatively simple empirical facts relating to crystallisation,

and consider also the limitless empirical facts of chemistry, we can see that the physical conceptions of extension and central forces connecting masses are nothing but imperfect representations of reality, however useful these imperfect representations may be within certain limits. The reality is far more than these conceptions can express.

From yet another point of view the abstract mechanical conception of a molecule is unreal. We now possess abundant evidence that molecules, just like crystals or other gross molecular aggregates, are in a state of constant decomposition and recomposition. So far may this process go in very dilute solutions of what are distinguished as electrolytes, that for all practical purposes their molecules hardly exist as such, and only the dissociated fragments are present. Thus a very dilute solution of sodium chloride or hydrochloric acid contains, practically speaking, only the ions formed by the dissolution of the molecules of sodium chloride or hydrochloric acid. I need, perhaps, hardly refer in detail to the very great significance of the conception of ionisation first introduced by Faraday, and the manner in which this conception has developed until it has transformed the whole outlook of both chemistry and physics. It is now evident that not merely gross aggregates, but also molecules and atoms, are in a state of constant decomposition, recomposition, and internal action. Their mass and extension appear to be nothing but an expression of this action ; and if so the distinction between matter and energy, or between structure and its activity, becomes only an imperfect representation of the actual world.

There are thus no real grounds for the contention that life must, in ultimate analysis, be capable of interpretation as a mechanical process. We must base our working conception of life on actual observation of living organisms, and certainly not on mechanical conceptions. Even from the purely physical standpoint, these are no longer adequate, but only provisional working hypotheses, useful for certain limited practical purposes, like the gas laws in either their original or amended form.

Empirical observations with regard to the behaviour of living organisms point clearly to the conclusion that in each detail of organic structure, composition, environment, and activity there is a manifestation or expression of the life of the organism regarded as a whole which tends to persist. It is this manifestation which distinguishes biological phenomena; and through all the temporary variations of structure, activity, composition, and environment it can be traced more and more clearly with every year of advance in biological investigation. We can trace it through the ordinary metabolic phenomena in living organisms, as well as through the phenomena of senescence, death, and reproduction. As it seems to me, it is only through the central working hypothesis or category of life that we can bring unity and intelligibility into the group of phenomena with which biology deals; and it is because the biological working hypothesis is for the present absent in our ordinary conceptions of physical and chemical phenomena that we must treat physical and biological categories as radically different. The popular and completely natural distinction between the living and non-living

is thus completely justified on the ground that biological observations cannot be expressed or described in terms of ordinary physical working hypotheses. For a more detailed discussion of this position in the light of the empirical facts of physiology I may perhaps refer to my recent book, *Organism and Environment*.

I must now pass to the question whether biological and psychological categories must also be treated as different. To this question it seems to me that there are still clearer reasons for returning an affirmative answer.

When we examine the organic wholeness and persistency which shows itself in the life of an organism we see at once that life is limited on all sides by what we can only interpret as physical and chemical conditions. If the oxygen percentage in the air breathed falls low enough, or the external temperature rises or falls sufficiently, life no longer dominates the phenomena. In every direction we see similar limitations.

A plant may be regarded as the type of what appears to be a mere organism. It is very sensitive to changes in its environment, and is helpless against numerous accidental changes, though human foresight can often quite easily guard it. A conscious organism is distinguished by the manner in which it overcomes these hindrances. It is aware of, and avoids, neutralises, or even takes advantage of them. It adapts its behaviour in such a manner as to maintain itself in the presence of what is outside the mere organic unity of its life. But in so doing the organism shows itself to be more than a mere organism: it includes within the unity of its life what seemed to be independent. In other words, the biological interpretation of the phenomena of

organisms is only a partial interpretation, just as the physical interpretation is a still more partial interpretation.

The reaction between a conscious organism and its environment is wholly different from the immediacy of what we interpret as physical or physiological reaction. In physical or physiological reaction one object reacts directly with another in space, but only in space: the reaction is immediate or "blind." Into conscious reaction, both the actual past and the potential future enter directly also. Objects of consciousness determine directly, and are determined directly by, past and future, as well as simultaneous, objects of consciousness. A psychological object is thus in dynamic relation with other objects surrounding it, not merely in space, but also in time. It has therefore an element of timelessness, inasmuch as it is in direct relation not only with present, but also with future and past objects. It involves action at a distance, not only in space, but also in time.

The physical world which we seem to see so plainly around us is reality as it appears in our consciousness. It is a reality of objects of consciousness, the constant presence of which guides all our conscious actions. What guides us is our *knowledge* of objects. This knowledge is there and constantly active, though the objects as physical or biological objects are out of sight or contact, so that their "immediate" influence is entirely absent.

It has already been pointed out that the world of mathematical physics is a very imperfect presentation of reality, and that in the biological world much more

of reality is presented. In the world of psychology still more of reality comes before us. The real world is not merely a physical or biological world, but also a *known* world. In identifying it as a known world we are making use of an additional category or working hypothesis. What makes this necessary is simply the nature of the empirical facts. A world which is not a known world means as little to us as a world in which the equation PV=RT holds good absolutely, or a world of atoms indifferent to one another. Such worlds are only ideal figments of our imagination, though the figments are very useful for certain limited purposes. In judging of the nature of reality we have no right to exclude the facts which emerge in either biological or psychological observation. It would be just as reasonable to exclude from physics or chemistry all the facts relating to ionisation. Conscious activity is a part of our objective universe, and must be taken account of in our judgments of reality.

Consciousness has been looked upon as a mere accompaniment of physical and chemical changes in nerve-cells. As has been already pointed out, the active changes within the living body cannot be interpreted as mere physical and chemical changes.

An alternative view is that conscious activity is a subjective accompaniment of what we interpret as vital activity. To me it seems clear that this view is not possible. Vital activity is "blind." This means that the organic unity which we can always identify in vital or biological activity is immediate in character. An unconscious organism adapts itself to new conditions, but only through a process which appears to be essen-

tially as blind as the action of gravitation. In the process of reproduction the germ might seem as if it were realising a conscious plan of the fully developed organism. Embryological investigation indicates, however, that each step in development is the immediate outcome of the conditions existing at the moment. If these conditions are abnormal the development will also be abnormal, so that all sorts of monstrosities are possible. It is true that for a mere organism the past lives on in the present, and there is a sense in which we can speak of organic memory. But we might equally describe this organic persistency as of the same nature as inertia. It does not present the character of conscious memory.

In perception and conscious reaction to it we are in contact with phenomena which we cannot interpret in terms of either physical or biological conceptions. An object which has been perceived is present to, and directly influences, both future and past objects of perception, so that their influence on conscious action is altered. When Faraday pointed out the existence of ions in solutions he made a discovery which has gradually exercised a more and more wide-spread influence on scientific and practical activity, and has at the same time given a new significance to previous discoveries. In every new act of perception, however unimportant, there is a similar influence on the reactions to future, present, and past perceptions. To what we regard as mere organism the past is simply a dead weight on the present, and the present on the future, just as in the case of what we regard as mere physical existence.

It has been assumed widely that, while we can

directly perceive physical or biological phenomena, we cannot perceive psychological phenomena directly, since they have no "objective" existence, and are only subjective accompaniments hidden behind, and possibly determining, objective physical and physiological changes. This assumption is baseless. The objective behaviour of a conscious organism or person is quite distinct from that of an unconscious organism, although at the lowest stages of consciousness the distinction may be so faintly marked that we are left in doubt, just as at the lowest stages of life we can hardly distinguish the living from the non-living. When we perceive a person it is most certainly a person, and not a mere organism, that we perceive. It is only by a process of abstraction from the full objective reality that we can regard him as a mere organism. The doctor or physiologist is constantly performing with great pains this act of abstraction, and the engineer or economist performs a still more violent act of abstraction when he regards the man as a motor or working unit, or as a weight to be carried. By a similar effort we can abstract from the objective reality of what is beautiful.

It is, of course, only by interpretation of our experience that we perceive psychological phenomena. But exactly the same is true of biological and physical phenomena. The physical realities which seem to lie so clear and solid in front of us are only bundles of interpretations in the light of previous and co-existing and anticipated experiences, all determining the existing experience. Even if, following Hume, we seek to disentangle the sensations forming the crude basis of these interpretations, we are no better off. The simplest sen-

sation carries interpretation with it, as Kant showed. The "objective" world is nothing but the world as interpreted in knowledge, and the physical or biological worlds are only abstractions from this objective world. Not only when we are observing psychological phenomena in other persons, but when we are studying natural phenomena of all kinds, is our world a psychological or spiritual world. Perhaps we realise this best when the progress of experimental science leads to a reconsideration of fundamental physical interpretations which, like those of mass, energy, or unchangeable atoms, have been employed without question for long periods. We have to go back to what was in the minds of those who established these interpretations.

I will now try to summarise the argument of this paper. When we make use of physical categories we are employing simplified maxims or principles which, on account of their simplicity, are very convenient for purposes of prediction, but which can only be used over a limited extent of our experience without gross error. When we attempt to apply them to biological or psychological phenomena, the error becomes apparent; we cannot express biological or psychological experience in terms of physical conceptions. In other words, we cannot reduce biological and psychological to physical categories.

Similarly, in biology we are also employing relatively simplified maxims which enable us to predict another large class of phenomena, but cannot be applied to what we distinguish as psychological phenomena without gross error. Hence we cannot reduce psychological to biological categories.

We may ask why, in interpreting the physical world, we make use of schematised conceptions which biological and even physical and chemical observations prove to be untenable. The reality behind atoms and molecules, for instance, is evidently far more than the schematised atoms and molecules of ordinary physics and chemistry. The answer is that for a large number of purposes the schematised conceptions are practically sufficient, and give us a short cut without which we should be helpless in practical affairs, since we have not the data for framing more adequate conceptions correctly. For biological phenomena the schematised physical conceptions are insufficient practically, and we must therefore make use of special biological conceptions, the relation of which to the physical conceptions must for the present remain more or less obscure for lack of data. It is the same as regards the relation of psychological to biological conceptions. For certain ordinary practical purposes we treat the biological and physical worlds as objective and independent of our knowledge of them; but this is only a convenient figment.

From the point of view of each individual science there is a conflict of categories or fundamental hypotheses with those of other sciences; but from the wider standpoint of philosophy these categories are only provisional working hypotheses. The world of our experience is a spiritual world, as already pointed out above; and this being so we must regard categories as only forms which the riches of this spiritual world pass through in the course of their ever fuller manifestation.

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